pp. 479-550] [May, 1947

TROPICAL DISEASES BULLETIN

Vol. 44.] 1947. [No. 5.

MAIN CONTENTS :

	PAGES
Summary of Recent Abstracts. IV. Trypanosomiasis	479–485
Malaria	486–505
Blackwater Fever	506
Trypanosomiasis	506–511
Leishmaniasis	511–512
Fevers of the Typhus Group	512–516
Yellow Fever	516–517
Dengue and Allied Fevers	518–519
Plague	519–521
Amoebiasis and Intestinal Protozoal Infections	521–525
Relapsing Fever and other Spirochaetoses	525–527
Yaws	527–528
Leprosy	528
Helminthiasis	529–531
Deficiency Diseases	531–532
Haematology	532–533
Venoms and Antivenenes	534–535
Dermatology and Fungus Diseases	535–538
Miscellaneous Diseases	538–542
General Entomology	542–546
Laboratory Procedures	546–547
Reports, Surveys and Miscellaneous Papers	547–548
Book Review	548–550

For detailed Contents see pp. ii [illegible]

IMPERIAL MYCOLOGICAL INSTITUTE
28 JUN 1947

Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.
(Telephone: MUSEUM 3041)

Price 3/6 net.] *Entered as Second Class Matter in the U.S.A. Post* Annual Subscription (Jan.-Dec.) 30/-

HONORARY MANAGING COMMITTEE

APPOINTED BY THE SECRETARY OF STATE FOR THE COLONIES.

Chairman: W. H. Kauntze, *C.M.G.*, *M.B.E.*, M.D., D.P.H., F.R.C.P. (*Chief Medical Adviser to the Secretary of State for the Colonies*).

Wm. Horner Andrews, D.Sc., M.R.C.V.S.

Lieut.-General Sir James Bennett Hance, *K.C.I.E.*, *O.B.E.*, M.D., F.R.C.S.Ed., K.H.S., I.M.S. (retd.).

Professor Patrick A. Buxton, *C.M.G.*, M.A., M.R.C.S., L.R.C.P., D.T.M. & H., F.R.S. (*representing the Royal Society*).

Sir Wilson Jameson, *K.C.B.*, LL.D., M.D., F.R.C.P. (*representing the Ministry of Health*).

Professor J. M. Mackintosh, M.D., F.R.C.P., D.P.H.

Sir Philip Manson-Bahr, *C.M.G.*, *D.S.O.*, M.D., F.R.C.P., D.T.M. & H.

Sir Edward Mellanby, *K.C.B.*, M.D., F.R.C.P., F.R.S. (*representing the Medical Research Council*).

E. R. A. Merewether, M.D., F.R.C.P., F.R.S.E., K.H.P.

Brigadier G. S. Parkinson, *C.B.E.*, *D.S.O.*, M.R.C.S., L.R.C.P., D.P.H., R.A.M.C. (retd.).

J. B. Sidebotham, *C.M.G.*, M.A. (*of the Colonial Office*).

Secretary: J. K. Creer (*of the Colonial Office*).

STAFF OF THE BUREAU:

Director: Charles Wilcocks, M.D., M.R.C.P., D.T.M. & H.

Assistant Director: H. J. O'D. Burke-Gaffney, *O.B.E.*, M.D.

Secretary: R. L. Sheppard.

LIST OF ABSTRACTERS IN THIS ISSUE.

A. R. D. Adams, M.D., Ch.B., M.R.C.P., D.T.M.
H. J. O'D. Burke-Gaffney, *O.B.E.*, M.D.
J. R. Busvine, Ph.D., B.Sc.
Professor P. A. Buxton, *C.M.G.*, M.A., M.R.C.S., L.R.C.P., D.T.M. & H., F.R.S. (*Sectional Editor*).
J. F. Corson, *O.B.E.*, M.D., D.P.H., D.T.M. & H.
Professor T. H. Davey, *O.B.E.*, M.D., D.T.M.
J. T. Duncan, F.R.C.S., L.R.C.P. (Ire.), D.T.M. & H.
J. D. Fulton, M.A., B.Sc., Ph.D., M.B., Ch.B., D.T.M.
Professor R. M. Gordon, *O.B.E.*, M.D., Sc.D., F.R.C.P., D.P.H.
Lieut.-Col. W. F. Harvey, *C.I.E.*, M.B., F.R.C.P.E., D.P.H., I.M.S. (retd.) (*Sectional Editor*).
Professor Edward Hindle, M.A., Sc.D., Ph.D., F.R.S. (*Sectional Editor*).
C. A. Hoare, D.Sc.
H. S. Leeson, F.R.E.S.
R. M. B. MacKenna, M.D., F.R.C.P.
Sir Philip Manson-Bahr, *C.M.G.*, *D.S.O.*, M.D., F.R.C.P., D.T.M. & H.
Professor B. G. Maegraith, B.Sc., D.Phil., M.B., B.S.
Maj.-Gen. Sir John W. D. Megaw, *K.C.I.E.*, D.Sc., M.B., B.Ch., I.M.S. (retd.) (*Sectional Editor*).
K. Mellanby, *O.B.E.*, Sc.D.
L. E. Napier, *C.I.E.*, F.R.C.P.
Sir H. Harold Scott, *K.C.M.G.*, M.D., F.R.C.P., D.P.H., D.T.M. & H.
H. S. Stannus, Ph.D., M.D., F.R.C.P., D.T.M. & H. (*Sectional Editor*).
R. Ford Tredre, M.D., D.P.H., D.T.M. & H.
J. Waterlow, M.B., B.Ch.
C. M. Wenyon, *C.M.G.*, *C.B.E.*, M.B., B.Sc., F.R.S. (*Sectional Editor*).
F. Norman White, *C.I.E.*, M.D., D.P.H., I.M.S. (retd.) (*Sectional Editor*).
Charles Wilcocks, M.D., M.R.C.P., D.T.M. & H.

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 44.] 1947. [No. 5.

SUMMARY OF RECENT ABSTRACTS.*

IV. TRYPANOSOMIASIS.

Epidemiology : Aetiology : Transmission.

DE AZEVEDO *et al.* (p. 828) have investigated the question of sleeping sickness in Portuguese Guinea, where they found 61 of 8,543 persons infected. *G. palpalis* is, apparently, the vector. They conclude that the effect of this disease on the general mortality is slight, and that the strain of *T. gambiense* is of low virulence.

WILDE and FRENCH (p. 1120) infected zebu cattle with *T. rhodesiense,* and kept them under detailed observation. They did not become seriously ill, but there was evidence that the trypanosomes were still present in the blood of some of the animals 6 months later. Cattle may therefore act as carriers of the disease.

BURTT (p. 1121) records observations on transmissibility and other features of *T. rhodesiense* after infection of an animal with a low body temperature (ant-bear). For the results and discussion the original should be consulted.

FULTON and STEVENS (p. 1121) have investigated the glucose metabolism of *T. rhodesiense.*

CAUBET (p. 312) has measured the trypanosomes of two strains of *T. gambiense,* which differ in the infections they cause in animals. One strain (Yaundé) was consistently longer (and less severe) than the other (Antwerp). The author thinks that the longer forms probably divide less quickly than the shorter forms. ROUBAUD (p. 419) discusses these measurements of the two strains referred to by Caubet, and states that the characters of the Yaundé strain have not varied since its isolation, which suggests that it is a special racial type ; it has marked neurotropic characters. It is possible that selection occurs in man when the infection passes from the early (blood and lymphatic) stage to the late (nervous) stage, and that the selected races are spread by tsetse in nature. This could explain the variations often observed in sleeping sickness areas. ROUBAUD *et al.* (p. 419) show that the Yaundé strain of *T. gambiense* has constant and strong neurotropic characters in white rats, whereas the Antwerp strain, which produces more acute infections, shows relatively little neurotropic tendency. STEFANOPOULO *et al.* (p. 417) have demonstrated that the neurotropic character of the Yaundé strain of *T. gambiense,* shown in the mouse and rat, is also apparent in the rabbit.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin,* 1946, v. 43. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

RODHAIN and RESSELER (p. 424) failed in attempts to distinguish schizotrypanosomes serologically from trypanosomes.

It is known that tsetse flies can be induced to salivate on a cover slip, and that trypanosomes in the saliva can thus be found. BURTT (p. 1121) shows that the chance of finding them is better if the cover slip is smeared with albumin. This is a relatively quick and simple method of identifying salivary infection.

BURTT (p. 827) has found that, if pupae of *G. morsitans* are kept, until they hatch, either in an incubator at 30°C., or at laboratory temperature below this, and if the flies which emerge are kept at laboratory temperature, and allowed to feed on animals infected with *T. rhodesiense*, the rate of infection is significantly higher in the flies from incubated pupae, and transmission experiments give more positive results. No difference in longevity of the flies was found. It is possible that this finding may have a bearing on the seasonal incidence of trypanosomiasis.

The same author (p. 828) found that, in his experiments, about twice as many male as female *G. morsitans* developed salivary gland infection. The reason is not clear, but it is possible that *G. morsitans* females do not survive mass confinement so well as males, and that there is a higher early death rate in females than in males.

JACKSON (p. 420) has shown that in nature (as in cage experiments) the male *G. swynnertoni* mates at random with female *G. swynnertoni* and *G. morsitans* ; the same is probably true of male *G. morsitans*. Yet though heterogamous matings are almost always barren, neither species appears to possess any mechanism to prevent their occurrence.

In an attempt to discover why different species of *Glossina* are found in different types of country, JACKSON (p. 312) introduced *G. morsitans* and *G. palpalis* into territory in which *G. swynnertoni* normally occurs. *G. morsitans* was able to produce a second generation, but *G. palpalis* was not. Neither could survive, but laboratory experiments designed to elucidate this fact suggested that the ability of each species to colonize a particular type of country is related rather to its behaviour (frequency of feeding, choice of resting place) than to straightforward physiological reaction to climatic conditions.

GASCHEN (p. 313) describes a method for determining, and expressing graphically, the climatic features which influence the various species of *Glossina*. He discusses the seasonal variation of *G. palpalis* and *G. tachinoides*.

KARTMAN *et al.* (p. 716) note that *G. palpalis* in French West Africa makes a characteristic buzzing noise during flight in the heat of the day. In Liberia and the Congo the flight of this species has been stated to be noiseless.

Pathology : Clinical Findings.

STEFANOPOULO *et al.* (p. 420) have found the " mulberry cells " of Mott in two of eleven white rats infected with the Yaundé strain of *T. gambiense*. In one they were present in brain tissue, in both in the spleen. These cells are probably not pathognomonic of trypanosomiasis.

GALLAIS (p. 633) has made a systematic description of the neuro-psychological forms of sleeping sickness, which bear a likeness to each other, and which result, fundamentally, from involvement of the region round the third ventricle. The symptoms may be classified as tropho-vegetative, psychic, motor and sensory. CHABEUF and MBAPPE (p. 1122) discuss the aetiology of certain chronic nervous (and in most cases mental) disturbances, mostly with grossly abnormal cerebrospinal fluid, seen in the French Cameroons, in an area where sleeping sickness is not common. They reach the tentative conclusion that many of these cases are, in fact, due to trypanosomiasis, though trypanosomes could not be found.

RIDLEY (p. 534) has examined the eyes of 215 West African patients suffering from trypanosomiasis. He concludes that inflammations due to the presence of trypanosomes in the tissues of the eye are rare and terminal; that ocular abnormalities, the commonest of which is papilloedema, are secondary to infection of the meninges and central nervous system; that concurrent onchocerciasis is common and ophthalmologically important, and that the risk of amblyopia, and even amaurosis, from therapeutic arsenic is serious. He (p. 1018) describes in detail the visual disturbances which may follow the use of pentavalent arsenical preparations, especially tryparsamide, in sleeping sickness; these may be evanescent, or lead to partial or complete permanent blindness. He thinks that impurities may be responsible for these effects, and stresses the importance of pure and fresh preparations, and of complete examination of the eyes before injection.

Treatment.

HARDING (p. 105) has made a careful study of the effects of treatment in a district of Sierra Leone, and for the purpose has followed up for 13–28 months (occasionally for 46 months) 2,713 cases of sleeping sickness. The drugs used were antrypol, tryparsamide, propamidine and pentamidine, in various combinations. He makes the point that the only reliable criterion of cure is the cerebrospinal fluid picture, and that the cell count is a more sensitive index than the total protein estimation; in assessing cure, he adopts 10 cells per cmm. as the normal limit. After discussing the effects of the different combinations and courses of these drugs, Harding makes the following rule, applicable for all occasions, "if it is convenient to arrange an interval of 3 weeks or more without treatment after the first dose of antrypol has been injected, then a further two of antrypol followed by five of tryparsamide are given; if the interval is between 2 and 3 weeks, only one further antrypol and six tryparsamides are given; and if the interval is less than 2 weeks, then no further antrypol is administered and the course is completed with seven doses of tryparsamide. This rule has since been applied over many thousands of cases, and it has been consistently found that no more than about 1 per cent. of patients die during treatment and no more than 1 per cent. become blind." The author has tried a combination of pentamidine with tryparsamide, and advises that this should be tried in other parts of West Africa, where the average case is less responsive to treatment with tryparsamide. He also gives evidence which suggests that antrypol and the diamidines, but not tryparsamide, exert, in addition to their curative action, a prophylactic effect which lasts for more than a year; but he makes the point that this is not necessarily true throughout West Africa. Nevertheless, the inclusion of one or other of these two drugs in courses of treatment probably reduces the danger to the community arising from the possibility of subsequent infectious relapse or reinfection among the treated persons.

LAUNOY (p. 423) from experiments on rabbits infected with *T. annamense*, concludes that they offered no evidence that albuminuria due to trypanosomiasis was a contraindication to treatment with moranyl [Bayer 205]. He reaches (p. 424) the same conclusion in relation to treatment with moranyl and anthiomaline simultaneously.

DEWEY and WORMALL (p. 830) show that Suramin [Bayer 205] combines rapidly with proteins, and that much of it found in serum is in combination with the proteins. Hydrolysed Suramin, however, does not combine with protein nearly so much. In comment, HAWKING states that there is some evidence that Suramin also combines with trypanosomes.

EAGLE (p. 421) produces evidence for the view that ionized salts of acid-substituted phenyl arsenoxides are much less active against trypanosomes than

the undissociated free acids. The relative trypanocidal activity of an acid-substituted phenyl arsenoxide is determined by, and is roughly predictable from :—(*a*) the *p*H of the solution ; (*b*) the *p*K of the compound ; (*c*) the trypanocidal activity of the ion. The higher the *p*K, and the lower the *p*H, the greater will be the observed activity of the compound. He notes that ions of weak acids or bases do not pass so readily through cell membranes as the corresponding undissociated molecules. The arsenicals here studied pass into the trypanosomes very rapidly, and form firm compounds with the cell constituents ; they are therefore removed from the diffusion equilibrium, and as a consequence, continued diffusion and concentration occur.

From a field trial of *p*-arsenosophenylbutyric acid in *T. gambiense* infections in Liberia, EAGLE (p. 1017) concludes that more than 90 per cent. of early cases may be cured within 2 weeks by 12–14 daily injections of 0·5 mgm. per kgm. of body weight, or within 1 week by 6–7 injections of 1 mgm. per kgm. The injections are usually given intravenously.

WEINMAN and FRANZ (p. 207) report on short-term results of treatment of trypanosomiasis in Liberia, with Melarsen oxide and a substance known as 70A. The conclusions are strongly criticized by LOURIE, who considers that the tests of efficacy admitted by these authors are not by any means stringent enough.

Experiments by ROUBAUD and CAUBET (p. 418) indicate that, in rats infected with a strain of *T. gambiense*, and treated with sulpharsenol as soon as trypanosomes appeared in the blood, some relative immunity, specific for *T. gambiense*, is developed.

CHEN and GEILING (p. 315) have assayed the anti-trypanosome effect of certain antimonials (using *T. equiperdum* as the test organism) by estimating the degree of interference exerted by the drug on glucose metabolism by the trypanosomes. By this method there is good agreement with results previously found by other *in vitro* tests for trivalent, but not so good for pentavalent, compounds.

LWOFF *et al.* (p. 313), have tested various derivatives of ethylene-diamine on cultures of flagellates, as regards correlation between findings *in vitro* and those previously made *in vivo*. Correlation varied according to the chemical composition of these substances, but for the rather complicated association of properties the original abstract should be consulted.

NELSON (p. 535) treated one patient, suffering from *T. rhodesiense* infection, with penicillin, which had no effect on the disease.

DUBOIS (p. 1087) has written a volume on the chemotherapy of trypanosomiasis, which deals in detail only with arsenicals and antimonials.

Control.

MCLETCHIE (p. 1022) has given a most informative account of the origin and development of the Anchau settlement in Northern Nigeria, in which systematic eradication of tsetse and settlement of population have taken place over a number of years. The many problems which had to be met in this great venture include not only medical, but also veterinary, agricultural and social problems, and much detailed investigation and supervision has been necessary to establish a now large and healthy population, with its stock, in this area of 700 square miles, free from tsetse. CLARKE (p. 1024) has also written a short account of the same work.

MORRIS (p. 537) shows how successful a large clearing experiment for the eradication of *G. palpalis* and *G. tachinoides* has been in the Northern Territories of the Gold Coast. In the dry season the flies are driven back to certain localized foci, and are associated with certain trees and shrubs (named in the original paper) ; these were cleared along several hundreds of miles of river, working down-stream, and the result has been a tremendous drop in the fly population,

a very great diminution in the incidence of sleeping sickness, and the opening up of 1,000 square miles of country. The old method of clearing the vegetation round water supplies and at river crossings was unsuccessful and has been abandoned. The reclaimed land is being developed satisfactorily. STEWART (p. 907) cleared *G. palpalis* and *G. tachinoides* from a valley in the Gold Coast by removing trees fringing the river. Erosion was feared afterwards, but did not occur ; the profuse growth of grass held the soil together, and the river never flows fast.

LEWILLON (p. 208) describes an easily constructed trap effective for *Glossina palpalis* ; for details the original abstract should be consulted. He claims that trapping is a practical method of control.

CHORLEY (p. 422), in a review of tsetse fly operations carried out in Southern Rhodesia during 1943, makes the point that intensive shooting of game may have highly beneficial effects on the control of *G. morsitans* in Portuguese East Africa.

The Trypanosomiasis Committee of Southern Rhodesia (p. 907) have issued a statement of the scientific basis of the control of *G. morsitans* by game destruction. This fly depends on the larger grazing and browsing mammals for its regular food supply, and if these are eliminated the fly is driven to extend such energy in the search for food that its death rate rises far above normal. It is, therefore, not necessary to destroy all species of animals on which the fly can feed, but only those on which it chiefly depends throughout the year. When this has been done, the fly cannot support life where grass is high and dense. *G. pallidipes*, which can find its prey even in thick vegetation, is much more difficult to control by these means.

HAVEAUX (p. 1019) has given a detailed account of 20 years of sleeping sickness control carried out by a mining group in villages of the Kasai region of the Belgian Congo. This control has, apparently, been entirely a matter of treatment, and of prophylactic injections of Bayer 205. Treatment at first consisted of injections of atoxyl, but later, Bayer 205 and tryparsamide were used, and the author gives details of the courses and doses employed, according to the condition of the patient. Results are analysed, and patients have been followed up for as much as 10 years ; the author thinks that sleeping sickness is easily cured in young people or in those in the prime of life, but not in older persons, under the existing local conditions. He notes that mass movements of the population, due to local wars, industrial development, etc., have conduced to the spread of the disease. There are no references to tsetse fly control.

VAN HOOF *et al.* (p. 536) conducted a controlled experiment on drug prophylaxis with pentamidine in a *T. gambiense-G. palpalis* village of the Belgian Congo, and conclude that one intramuscular injection of 3 mgm. per kgm. body weight will protect a healthy person for at least 6 months. In comment, CORSON suggests that a planned experiment with volunteers and isolated infected flies might reduce some of the unknown factors in the authors' work.

Trypanosomiasis of Animals.

FIENNES (p. 16) describes what he believes to be micro- and macro-gametes of *T. congolense*, in a drop of infected blood to which a drop of 0·3 per cent. sodium chloride solution had been added, and their conjugation to form oöcysts, zygotes and sporozoites. He gives details of the appearance of the structures described.

WIEN (p. 716) has tested 19 diamidines and 9 phenanthridinium compounds for activity against " acute " and " chronic " strains of *T. congolense* in mice. The outstanding compound was phenanthridinium 1553, which has already given promising results in cattle in Uganda [CARMICHAEL and BELL, this *Bulletin*, 1945, v. 42, 259], and which has an index of 152 when tested against

an acute strain of *T. congolense.* Its pharmacological action is depressant on the circulation and respiratory centre, and in high doses it is toxic to the liver and kidneys.

LAUNOY (p. 314) shows that *T. congolense* (a species with much natural resistance to drugs) and a strain of *T. annamense* which has acquired resistance to some antimonials, behaved differently when treated in guineapigs by drugs of the diamidine group. *T. congolense* infection was little influenced by them.

It is known that Bayer 205 and certain amidines have a prophylactic effect against trypanosomiasis. FRIEDHEIM and BERMAN (p. 1124) now describe a pentavalent antimonial which has shown prophylactic and curative action against *T. equiperdum* in mice. This effect may be due in part to an immunological factor, and MAYER and BROUSSEAU (p. 1125) produce evidence to show that this is probably so. The immune property of infected and treated mouse blood is probably connected with the death of the parasites. The authors discuss the matter.

SCHATZ *et al.* (p. 1025) have found several soil fungi which produce filtrates active against *T. equiperdum in vitro*, but not active against bacteria.

AUGUSTINE (p. 1025) has shown that in *T. lewisi* infection of rats, immunity to reinfection depends upon a humoral trypanocidal antibody, to which developing parasites are particularly susceptible.

Chagas's Disease.

MARTINS *et al.* (p. 718) have made an interesting epidemiological study of a focus of Chagas's disease in Minas Geraes. The people live in mud and wattle hovels, most of which harbour the vector bugs. Of 146 persons, 33 were infected, and dogs, cats and armadilloes were also found to be infected. *Panstrongylus megistus* and *Triatoma sordida* were found, and a high proportion were infected. MOSELEY and MILLER (p. 316) note that Chagas's disease is rare in the Panama district, but describe two cases in American soldiers, contracted there.

LITTLE and SUBBAROW (p. 538) describe a medium for the cultivation of *T. cruzi* in large volumes ; for details the original must be consulted.

ROMAÑA and TERRACINI (p. 110) have succeeded in infecting mice with *T. cruzi* through the apparently intact skin.

DIAS and DE FREITAS (p. 108) contribute a first paper on the biometrical study of haemoflagellates of the genus *Schizotrypanum*, which are parasites of various mammals. Certain measurements are discussed, and assessed in relation to their importance for determining species.

DIAS and TORREALBA (p. 109) claim to have isolated *Trypanosoma rangeli* from man in Venezuela. This parasite had previously been found in Triatomid bugs, but the vertebrate host was, apparently, not known. In comment, HOARE suggests that elucidation of certain points is needed before the authors' conclusions can be accepted.

FLOCH and DE LAJUDIE (p. 908) have found *T. cruzi* in *Rhodnius pictipes*, *R. prolixus* and *Triatoma rubrofasciata*, in French Guiana.

FULTON and HARRISON (p. 1123) describe an outbreak of *T. cruzi* infection in monkeys recently imported from India. They discuss the possible mode of infection, and do not exclude the possibility of laboratory infection. In comment, HOARE remarks that in two of the laboratories concerned, *T. cruzi* is maintained in rodents, and in one, bed-bugs are present in the animal house. It seems that transmission may have been effected by these bugs.

MARTINS *et al.* (p. 718) note that xenodiagnosis has proved to be the most reliable test in chronic Chagas's disease. They have used laboratory-bred *P. megistus*, *T. infestans* and *T. vitticeps* for the purpose, and by this means have found considerable numbers of positive results in groups of patients suspected of

the disease, including some with myocarditis and some with megaoesophagus.

LIEM and VAN THIEL (p. 719) have prepared a dried antigen from a culture of *T. cruzi,* for use in a complement fixation test in Chagas's disease. The test was positive in a few controls—patients with positive Wassermann, or suffering from chancroid—but the authors suggest that the antigen should be tried out in known cases of Chagas's disease in South America.

LARCHER and ROMAÑA (p. 110) describe the appearance of the local swelling associated with infection by *T. cruzi* through the bite of a Triatomid bug. This is red, oedematous, hard, and slightly painful on palpation, and may take one of various forms. The associated glands contain developmental forms of *T. cruzi.* MAZZA, MIYARA and JÖRG (p. 208) describe in detail the histological changes in portions of the conjunctiva taken by biopsy in the early stage of Chagas's disease. Details of these changes are given in the original abstract. The authors found leishmanial forms of *T. cruzi* in nodules of the conjunctiva of a man who had been bitten on the eyelid by an infective bug.

MAZZA (p. 831) again stresses the fact that any association between Chagas's disease and goitre or cretinism is entirely fortuitous.

DIAS (p. 830) describes 254 cases of Chagas's disease seen in Minas Gerais ; abnormal electrocardiograph records were found in 97. TORREALBA (p. 831) notes that although other causes of myocardial disease occur in the rural population of part of Venezuela, the commonest is Chagas's disease. He quotes cases of sudden death from this cause. RAMOS and LAUS (p. 909) describe six cases of myocarditis in Chagas's disease. BRASIL (p. 908) has given a succinct account of the chronic cardiac lesions in Chagas's disease. ROMAÑA (p. 111) has found *T. cruzi* in the valves of a dog's heart.

BORGES-FORTES (p. 316) describes the acute lesions of the nervous system which may occur in Chagas's disease, with early localization of the parasites in meninges, brain or medulla, the primary site being in the neuroglia cell. He also describes the degenerative foci of the chronic form, which may be found in the cortex and the caudate and lenticular nuclei, and the inflammatory and degenerative foci in the meninges.

MAZZA *et al.* (p. 909) describe small, punched-out ulcers, papular eruptions and other cutaneous manifestations of Chagas's disease.

PÉREZ and ROMAÑA (p. 112) describe a patient who has had Chagas's disease for 20 years, and is now, apparently, a simple carrier ; and a case of spontaneous cure.

BROWNING *et al.* (p. 633) describe two phenanthridinium compounds which show activity against *T. cruzi* in mice, comparable with that shown by the compound Bayer 7602 (Ac). The degree of activity, though the best yet encountered, is still not of a high order. The correct composition of Bayer 7602 (Ac) is disclosed in a comment by LOURIE. MAZZA *et al.* (p. 720) give good reports of the British equivalent of the German preparation Bayer 7602 (Ac), and also of penicillin, in Chagas's disease.

TALICE and LÓPEZ-FERNÁNDEZ (p. 112) report on the use of *p*-arsenophenyl butyric acid in Chagas's disease, but not very optimistically. This drug has been used, with some moderate success, in African trypanosomiasis.

TALICE (p. 112) notes that penicillin was quite useless in one case of Chagas's disease, which confirms the experiments made in animals.

ENGEL (p. 111), unlike some previous workers, has failed to observe any tendency towards cure of a certain new growth of mice by treatment with a toxin prepared from *T. cruzi.* *Charles Wilcocks.*

MALARIA.

SANJUAN FUENTES, J. Notas sobre el paludismo en la zona de Tanger. [**Malaria in the Tangier Zone.**] *Med. Colonial.* Madrid. 1946, Dec. 1, v. 8, No. 6, 430–44, 3 graphs & 1 map.

In 1942 there was a marked increase of malaria in the Tangier Zone (as there was in adjacent parts of North Africa). The author gives an account of the incidence of the disease during the three succeeding years, 1943–1945, excluding the City of Tangier. An outline of the topography and meteorology of the country is given. The numbers of cases of malaria seen in the three years were 637, 175 and 39 : the marked decline in incidence is attributed to the wider use of suppressive medication and hygienic measures. The vast majority of infections were *P. vivax* ; 3·9 per cent. were *P. falciparum.* No *P. malariae* infection was seen. No information is given about the anopheline vectors.

Norman White.

GEVORKOV, A. A. [**Correction of Dynamic Curves of Primary and Relapsing Malaria in the Samarkand District.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 31–4. [In Russian.]

The author has undertaken a statistical analysis of the official records of malaria in the Samarkand region of Central Asia, where a large number of relapses are recorded for the first and second half-years. The material for this study was based on the data of the regional tropical stations for the years 1940–1944, on the parasitological characteristics of malaria incidence in this region, and on the incidence in districts where malignant tertian malaria is predominant. According to these data, from 5 to 12 per cent. of the cases occurring during the first half-year represent primary infections with a long incubation period, while the majority of so-called relapses in the second half-year represent re-infections, their proportion amounting to more than 80 per cent.

C. A. Hoare.

GUYANE FRANÇAISE : RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR DE LA GUYANE FRANÇAISE ET DU TERRITOIRE DE L'ININI PENDANT L'ANNÉE 1945 [FLOCH, H., Director]. (Publication No. 125. 1946. Cayenne.) pp. 53–62, 1 fig. Paludisme. [**Malaria.**]

The examination of schoolchildren in three localities, St. George's (Oyapock), Ouanary and Kourou, revealed spleen rates of 38, 37 and 55 and parasite rates of 26, 20 and 31 respectively. The capital Cayenne is all but free from endemic malaria except in the outskirts and even here conditions have been improved by reclamation. Twenty species of Anopheles have been identified in French Guiana : *A. nimbus, A. acanthotorynus, A. kompi, A. canorii, A. eiseni, A. intermedius, A. mediopunctatus, A. maculipes, A. peryassui, A. aquasalis, A. nunez-tovari. A. oswaldoi, A. pessoai, A. darlingi, A. strodei, A. ininii, A. sancti-elii, A. triannulatus, A. neivai,* and *A. squamifemur. A. darlingi* is the most important vector of malaria in French Guiana ; it has not been captured in Cayenne where anophelines formed but 0·6 per cent. of all mosquitoes captured during a six-year period. In 1945, 80 per cent. of positive blood smears contained *P. falciparum,* 20 per cent. *P. vivax.* In previous years, *P. malariae* infections were occasionally found but they are rare. The period of maximum malaria incidence is the dry season, August to October inclusive ; incidence is lowest in February, the most rainy month. *Norman White.*

FONSECA, F., CAMBOURNAC, F. J. C., PINTO, M. R., PEREIRA, J. M. & CUNHA, A. **Studies on the Exo-Erythrocytic Cycle of Malaria.** *Parasitology.* 1946, Aug., v. 37, Nos. 3/4, 113–17, 23 coloured figs. on 1 pl. [36 refs.]

The studies described in this paper cover attempts to infect chicken embryos by various routes with *Plasmodium gallinaceum* and efforts to discover exo-erythrocytic stages of development in the bone-marrow of general paralytics, in the spleen and other organs of persons who had died shortly after receiving malaria therapy or in the spleen of malaria patients during the latent period preceding relapse.

In the case of *P. gallinaceum*, after deposition of sporozoites on the chorio-allantoic membrane following scarification, about half of the 15 embryos so treated survived and developed to maturity. All the chicks died, however, 24 hours after hatching : exoerythrocytic stages of development of the parasite were found in the brain, bone-marrow and liver. They were often most numerous in the liver. Chicks inoculated with infected liver emulsion acquired an exoerythrocytic infection followed by an erythrocytic one. Deposition of blood rich in erythrocytic forms on the membrane resulted in infection in only one of six chicks which died on the 4th day after hatching. Erythrocytic forms alone were found. When the infective blood was inoculated into a vessel on the membrane, infection, presumably of the erythrocytic type, developed in all instances. It was fatal either before or a few days after hatching. No infections followed the injection of blood into the yolk sac. Smears made at various intervals (8–24 hours) from the area of the chorio-allantoic membrane on which sporozoites had been deposited revealed minute blue-staining bodies with one, two or three chromatin dots and one larger one with eight such dots. Most of these were intracellular. The authors conclude that they represent the intracellular forms developed from sporozoites.

Four paralytic patients were infected with *P. vivax* and three with *P. falciparum* by the bites of infected mosquitoes and the injection of emulsion of infected salivary glands. Bone-marrow and peripheral blood films made on the third, sixth and ninth days were entirely negative. Three other general paralytics were subjected to *P. vivax* sporozoite infection and on the fourth and eighth days following injection, two groups of three other patients were sub-inoculated. On each occasion the following inoculations were made. One received intrasternally 5 cc. of blood and bone-marrow obtained by sternal puncture, another intramuscularly a similar injection and the third 20 cc. of venous blood intramuscularly. It is not quite clear whether in the sub-inoculations each patient received blood from a single primary case or the pooled material from all three. However this may be, only two of the three primary cases became infected and none of the six secondary ones. In the smears of the bone-marrow, no definite exoerythrocytic forms could be found. It is concluded that the negative results show that if such are present they must be exceedingly rare.

It was noted that parallel examinations of the bone-marrow and blood showed that erythrocytic parasites usually appeared first in the blood, where they generally remained more numerous than in the bone-marrow. From this it is concluded that the bone-marrow is not likely to be the principal seat of development of exoerythrocytic stages. Accordingly when patients with various diseases who had been subjected to malaria therapy by sporozoite infection died within a few days a careful examination of the spleen, liver, lungs, brain and bone-marrow was carried out. Some of these examinations revealed forms which were comparable with the small stages having one or two chromatin dots seen in the chick embryo experiments. Thus in *P. vivax* cases in which death occurred five and eight days after injection such forms were found in the

spleen intra- and extracellularly. Similar forms were found in the spleen of a *P. falciparum*-infected patient who died on the eighth day. In all these cases, the post-mortem examinations were conducted from six to 24 hours after death.

Attempts were then made to discover exoerythrocytic forms in malaria patients in whom relapses could be anticipated. It is remarked that relapses in benign tertian malaria not infrequently follow blood-induced infections and that they are not so rare as some observers think. It has been noted that when malignant tertian malaria is treated with cibazol (a sulphathiazole) there results a cessation of the fever and disappearance of schizonts, followed by increase in the sexual forms. Later relapses nearly always occur. Accordingly spleen puncture was performed on 10 patients after cibazol treatment. In smears of the spleen material, a few small intracellular forms with one or two chromatin dots were found. Similarly in the spleen of a case of benign tertian malaria similar forms were seen. The various forms found in these investigations are clearly depicted on a coloured plate.

The general conclusion of the authors is that their researches have convinced them that in human, as in avian, malaria, there is a reticulo-endothelial cycle which precedes the erythrocytic phase. They admit, however, that a complete proof of its existence can only be accepted when forms resembling the micro- and macro-schizonts of avian malaria have been found. [With this conclusion the reviewer agrees, for it seems to him that the small pigmentless forms with one or two chromatin dots might be merozoites from an erythrocytic schizogony which were still extracellular or had been phagocyted by macrophages.]

C. M. Wenyon.

See also p. 542, MER, BIRNBAUM & AIOUB, **The Attraction of Mosquitoes by Human Beings.**

IVANOVA, L. V. [**Light Reactions of Anopheles Larvae on a Moist Surface.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 53–5, 2 figs. [In Russian.]

It is known that under natural conditions larvae of *Anopheles* are capable of crawling over moist surfaces when escaping from a drying pool in search of water.

Working with crawling larvae of *A. maculipennis atroparvus*, *A. m. messeae* and *A. superpictus* belonging to stages III and IV, the author studied their reactions to light. It was found that white light provokes in them a reaction of negative phototaxis, manifested by the anterior part of the body turning or the larva moving away from the source of light, the movements of the larva being independent of the direction of gravity, while photokinesis is shown by increased activity of the larvae. In the case of red light, the larvae become less mobile (elimination of photokinesis) and the trajectories of their paths become strongly convoluted, but there is no change in the orientation of the larvae in relation to the source of light ; on the other hand, they are affected by gravity, for they refuse to crawl up a declined surface. It was thus shown that the reactions of crawling anopheline larvae to light differ markedly from their reactions when in water in that the sign of phototaxis is positive in the latter case, and negative in the former.

C. A. Hoare.

TREDRE, R. F. **The Rôle of** *Anopheles gambiae* **var.** *melas* **in the Transmission of Malaria in the Vicinity of Freetown Estuary, Sierra Leone, 1943.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 380–420, 2 maps, numerous graphs & diagrams & 21 figs. on 5 pls. [15 refs.]

The author carried out, in the vicinity of Freetown, a careful investigation of the importance of *A. melas* as a vector of malaria, the results of which he

describes, together with an account of the methods and effects of the control measures employed.

In Freetown the progress of sanitation since its inauguration by Ross in 1901 has effected a great reduction in malaria resulting in delayed development of immunity in the children and an increasing incidence of clinical malaria in the adult African inhabitant. In the villages, however, near which large numbers of the armed forces were of necessity accommodated, malaria was uncontrolled until the recent war, spleen rates in children varied from 32 per cent. to 76 per cent. and immunity was acquired in childhood, adult malaria being rare.

Investigation of the house-frequenting anophelines had shown that they included a large proportion of melanic *gambiae* with either three- or four-banded palps, but, until the work described in this article, no attempt was made to control this saline-water breeding species. MUIRHEAD THOMSON's description of the egg and recognition of the main breeding places of *A. melas* as being in the belt of Paspalum and Avicennia mangrove in tidal marshes was fundamental to the present investigation. Pool formation in this zone depends on tidal inflow occurring at average spring tides, but in the wet seasons seepage helps to maintain a bog-like condition with pooling in the grass. It was found that *melas* eggs were laid in the sea-grass belt and adjacent area of Avicennia, and that larvae congregated in the Avicennia zone where they matured ; the aquatic stages are not found in Rhizophora mangrove. As a result of these conditions *melas* production rises rapidly at the onset of the rains, reaching a peak in a few weeks. The heavy rains cause a decrease in breeding, which rises again as the rains diminish ; and a high production is maintained until towards the end of the dry season when it falls to a low level. These data indicated where and when dense *melas* breeding could be anticipated and where control measures could be expected to cause a reduction in malaria transmission, particularly during the dry season when the breeding of *gambiae* " type " was minimal.

Aerial photographs of the mangrove forests round Freetown identified the " orchards " of Avicennia which were found to form only a small proportion of the total. These orchards were visited and all those near African dwellings were found to be producing *A. melas*. The most productive areas included two which were easy of access from Freetown and were near the villages of Aberdeen and Wellington ; in these were studied the density and infectivity of *A. melas* and the results of control by exclusion of tidal waters.

Random collections of house-frequenting anophelines were made throughout the year in the village of Wellington. Of 2,003 specimens of the *A. gambiae* group, 461 were four-banded, 1,009 were three-banded, and 533 had the palps too rubbed for identification. Those in this last category and the three-banded specimens were set individually to lay eggs on filter-paper moistened with 50 per cent. sea water and the eggs were identified. Of the 1,009 three-banded specimens 486 produced *melas* eggs, 26 produced " type " eggs, while of the 533 unclassified 133 were *melas* and none produced " type " eggs. Identification by the characteristics of the eggs showed that in Wellington the ratio of four-banded to three-banded *melas* was 1 : 2·7. This ratio was used to estimate the proportion of *A. gambiae* and *A. melas* among anophelines of the *A. gambiae* group collected in adult catching stations.

A total of 1,000 *A. melas* were dissected ; 4·2 per cent. were found infected in the salivary glands and 4·7 per cent, showed oöcysts. The peak density of infective *A. melas* was found to be in June when density of the species was greatest, and the maximum sporozoite rate was recorded in March when *melas* density was almost at its lowest. The predominant house-frequenting anopheline in various villages along the south shore of the estuary was *A.*

gambiae " type " with the peak density in June and July. *A. melas* formed one-quarter to one-third of the total anopheline population during the wet season and its density remained constant from September to January, during which time *A. gambiae* fell to below that of *melas*. No other anophelines were present in significant numbers.

Two methods of *A. melas* control were investigated. Where the terrain was suitable (*e.g.*, a village at the end of a peninsula) it was found that removal of the inhabitants within a two-mile radius of the *melas* producing zone reduced breeding almost to the point of elimination. This method was employed for military purposes on two occasions. The control measure mainly used was the exclusion of tidal water from the upper parts of the tidal area where it consisted of a belt of Paspalum grass and Avicennia mangrove. This method was employed experimentally in the creek adjacent to Aberdeen village in which there was an isolated area of Avicennia mangrove of some 100 acres supporting heavy *melas* breeding. During the dry seasons of 1942 to 1944 an embankment, higher than high spring tides, was built with soil dug from a wide shallow perimeter drain just internal to the bund which passed through the mangrove, cutting off two-thirds of the Avicennia orchard from the tide. An intercepting drain was cut to carry seepages into the perimeter drain which discharged through the bund by means of a sluice gate with tidal flaps. In a similar operation at Wellington village a mechanical ditcher was used to excavate the drain and provide soil for the bund.

Subsequent observations showed that in the dry season there was no pooling in the bunded area and consequently no breeding. In the wet season, pool-formation occurred at Aberdeen as a result of heavy rain and an inadequate sluice gate, but no *melas* breeding was found though *A. gambiae* " type " bred freely. Pools in the perimeter drain produced no larvae probably because of the presence of larva-eating fish. *A. melas* breeding was detected in man-made pools in the Avicennia external to the bund. The effects of control measures, which included adult mosquito destruction in the villages during the whole period, the use of larvicides during 1941 and 1942 and the control of the swamps and seepages, were reflected in the returns from adult catching stations over three years. The anopheline room index which had been 7·31 on weekly catches in 1941 fell to 2·22 in 1943. The ratio of *A. gambiae* to *A. melas* altered from 1 : 62 in 1942 to 1 : 1·8 in 1943. These results justified the extension of bunding as a control measure to similar breeding zones on the shores of the Freetown estuary.

Much detailed information is contained in the many tables, figures and diagrams forming appendices to the paper, and numerous excellent photographs illustrate the breeding grounds of *A. melas* and the various stages in the control measures. *T. H. Davey.*

USTINOV, A. A. [**Observations on the** *Anopheles bifurcatus* **L. in Abkhasia.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 50–53, 2 figs. [In Russian.]

The author records observations on the ecology of *Anopheles bifurcatus* carried out in Abkhasia on the Black Sea coast of the Caucasus, where this is the commonest species of mosquito.

In the coastal area, the maximum numbers of this mosquito are encountered in spring and in autumn, while in the mountain zone they are more common in summer. The adult is absent from the coast only during the two winter months (January and February). The larvae develop throughout the winter, reaching stage IV by March. Only the larvae are oligothermic and are unable to develop in warm water, whereas the high summer temperatures have no depressive effect on the imago. The gonotrophic correlations point to the absence of

autogenous development of the ova and to reduced exophily of *A. bifurcatus* in Abkhasia. The age composition of the mosquito population is very young and is not subject to much variation in different months. *C. A. Hoare.*

USTINOV, A. A. [**Seasonal Changes in the Age Groups in the Population and Gonotrophic Cycles of** *Anopheles maculipennis maculipennis* **in Abkhasia.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 44–9, 4 figs. [In Russian.]

The author describes the results of investigations on *Anopheles m. maculipennis* carried out between 1937 and 1940 in Abkhasia (Caucasus) and summarized in a number of tables and graphs.

The seasonal changes in the age-groups within populations of mosquitoes are determined by variation curves of the dimensions of the ampullae of the oviducts. It was found that in the humid subtropical zone of the Soviet Union the mosquitoes live longer than in other parts of the country, on account of which the campaign against the adult stages is of greater importance in this region. The sexual activity of the females can be observed in the course of 10 months (from February to November), but solitary females with developing ova may be encountered even in December and January. Already in October and even in September some of the mosquitoes are in a state of gonotrophic dissociation: in spite of blood meals, the ova do not develop. This circumstance provides conditions favouring infections inside houses, but the actual existence of such infections has not so far been observed in Abkhasia.

C. A. Hoare.

WHITE, R. Senior & RAO, V. V. **Orissa: from Pleasaunce to Pathological Museum.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 297–308. [15 refs.]

The authors confine their attention to the three plains districts that constitute Orissa proper and seek to explain how a country, which long ago had a reputation of being "a model of ancient prosperity", has degenerated to being the home of a poverty-stricken and disease-ridden peasantry. If ever Orissa merited its title of "The Glorious Country" it was before the fall of the Lion dynasty in the sixteenth century. The British took over a province ruined administratively, agriculturally and physiologically and at a time when river degeneration was rendering, not only control of floods, but even access to the province by sea, increasingly difficult.

Senior White and his colleagues have shown that *Anopheles annularis* is the principal vector of malaria in the plains of Orissa, inland from the coast. *A. annularis* has a wide geographic distribution, from the Indus to Formosa, but it is only in the Orissa plains that it is the principal vector of malaria; it is a zoophilous species. In Orissa, conditions favour a particularly heavy growth of aquatic vegetation in innumerable village tanks among which *A. annularis* larvae find perpetually favourable conditions. Each rains, *A. annularis* spread from tanks to ricefields; the water in ricefields is diluvial; there is no irrigation. The neighbourhood of rice fields on the New Alluvium, where water stands for long periods, is intensely malarious. The Bengal-Nagpur Railway has shown how malaria incidence can be reduced by cleaning, and keeping clean, village tanks.

Near the seaboard of Orissa, *A. sundaicus* is a more dangerous vector of malaria than is *A. annularis*. There are numerous villages only a few feet above mean sea level from which the tides are excluded by salt *bandhs*. If such areas become flooded their rapid drainage is impossible; *A. sundaicus* flourishes but its presence and density are very variable.

These brief extracts make no pretence of being a summary of an interesting paper: an epitome of the historical facts and speculations produced is not possible. *Norman White.*

YOUNG, M. D., ELLIS, J. M. & STUBBS, T. H. **Studies on Imported Malarias. 5. Transmission of Foreign** *Plasmodium vivax* **by** *Anopheles quadrimaculatus*. *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 477–82.

This paper describes the attempted transmission of strains of *P. vivax* of foreign origin, South Pacific, Mediterranean and Burma, by *A. quadrimaculatus* to 186 men, 151 white and 35 negro. They were all neurosyphilitics except for 14 white volunteers. Among the 151 white patients, 94·7 per cent. were infected, 92·1 per cent. on the first attempt. Of the 35 negro patients, only 31·4 per cent. were infected, 28·5 per cent. on the first attempt. The negroes exhibited a resistance to strains from all areas. All strains had a high infectivity rate for white patients. In 3 white patients, recent infection with a local strain of *P. vivax* did not prevent infection with a foreign strain.

Norman White.

MELENEY, H. E. **The Physiological Pathology of Malaria.** Reprinted from *Publication No. 15 of Amer. Ass. for the Advancement of Science.* 1941, 223–30.

This paper is a short review of the "physiological changes produced in human subjects and experimental animals by the various species of malarial parasites." The author deals briefly with the possible clinical effects of the continuous repetition of schizogony in the blood-stream and then considers in more detail certain changes in the physiological pattern of the infected animal. Total serum protein is generally reduced in both the acute and latent stages of malaria. Albumin is affected most; total globulin is often increased and the proportion of euglobulin always. Some authors have found these changes most pronounced during and after the paroxysm. Alteration in sedimentation rate and other physico-chemical changes in blood reported in malaria and the appearance of positive serological tests for syphilis are discussed in relation to changes in blood protein. Blood cholesterol has been found to increase during the rigor in human malaria and to fall slightly in *P. knowlesi* infection in monkeys. In the latter, however, cholesterol rose when the infection was overwhelming and where haemoglobinuria occurred as a terminal event. Some authors have suggested that cholesterol might therefore possess an inhibiting influence on haemolysis. This has not been confirmed experimentally. Lecithin concentrations follow those of cholesterol.

A rise in blood sugar has been reported during fever in *P. vivax* and *P. falciparum* infections. This rise might result from increased glycogenesis, such as is seen in protein shock. In this connexion, decreases in both laevulose and galactose tolerances have been observed in malaria. The principal change in blood electrolytes observed in malaria is a rise in plasma potassium, seen especially in *P. vivax* infections and occurring in the early stages of the paroxysm. In monkeys, similar rises in potassium were observed at the time of sporulation. The increase in potassium was greater than could be explained by the destruction of erythrocytes, so that some appeared to come from tissue cells. The clinical effects of malarial invasion may be related to the toxicity of high plasma potassium concentration. Adrenal hypofunction possibly resulting from the high blood potassium may also be concerned in the production of the clinical picture. The chemical composition and possible rôle of haemozoin and other pigments are discussed.

The anaemia in malaria is usually of the secondary type, although primary anaemia has been described. Progressive reduction in erythrocyte numbers leads to corresponding loss of the oxygen-carrying capacity of the blood and tissue respiration is thus probably interfered with. Clinical observations have shown that the circulation is often profoundly affected in malaria, particularly in *P. falciparum* infections. Such circulatory changes may be due to " plugging of capillaries " by parasitized red cells and the " liberation of toxic substances from these erythrocytes on the completion of schizogony." The plugging of capillaries probably accounts for many of the severe symptoms of *P. falciparum* infections. The progressive blood destruction, pigment metabolism and interference with circulation seen in malaria place heavy burdens on the organs, especially the liver and kidneys. Functional changes in both organs have often been reported during malaria. The author considers that the acute renal failure of blackwater fever results chiefly from mechanical obstruction of the kidney tubules.

[This paper is disconcertingly brief. The literature reviewed is limited, but the subject is one of absorbing interest and importance.] *B. G. Maegraith.*

TALIAFERRO, W. H. **The Cellular Basis for Immunity in Malaria.** Reprinted from *Publication No. 15 of Amer. Ass. for the Advancement of Science.* 1941, 239–49, 2 pls.

This is a short restatement of the cellular aspects of the host response to malarial invasion. Studies of tissue obtained from monkeys infected with malaria have revealed cellular activities which are usually missed in the examination of human material in which serial studies are not possible and degenerative changes tend to predominate. The characteristics of malarial immunity are determined in the first case by the localization of the parasites in certain tissues and the cellular response shows itself in four ways: phagocytosis; the production of new phagocytes; reparative proliferations; the production of specific antibodies.

The author deals with the first three of these responses. A careful account of the cells involved is given, based mainly on the results of histological investigations in simian malaria. The active cells are mainly mesenchymal in origin and are found in the blood and lymph, the reticular or blood forming tissues and the widely dispersed loose connective tissue. The functional importance of these cells is dependent on their wide distribution, their capacity for phagocytosis, their ability " to secrete enzymes and antibodies " and their varying powers of development into other forms of cells.

Fixed macrophages, which are defined as any large phagocytic monocytes, or any such cells which are capable of becoming immediately phagocytic, are derived mainly from reticular cells, littoral cells, *e.g.*, those lining the sinusoids of the liver, pericytes and the macrophages (histiocytes, clasmatocytes, resting wandering cells, and rhagiocrine cells) of connective tissue. The endothelial cells of the blood vessels are only rarely phagocytic and do not usually become so. *Free macrophages* include lymphoid cells in addition to those in the lymphatic tissues. These cells are similar to lymphocytes but are probably the stem cells of myeloid cells. Under normal conditions they reproduce myeloid cells, and lymphocytes reproduce lymphocytes, but under abnormal stimulus, as in malaria, both may develop into any type of mesenchymal cell. In the author's view " the lymphocyte is probably the single most important source of new macrophages in malarial immunity." Hyperplasia of the reticulo-endothelial system (*i.e.* the macrophage system) is frequent in malaria. The author considers that the newly-formed macrophages come principally from lymphocytes within what he terms the " lymphoid-macrophage system ",

which includes macrophages (as above), lymphocytes, Maximow's polyblasts and many of the cells seen in inflammatory processes. Fibroblasts and vascular endothelial cells are highly differentiated in man and monkeys and their function in malarial immunity is probably restricted to repair and reproduction of their own cell types.

Malarial immunity reactions are primarily parasiticidal. Parasites from the beginning of the infection exhibit a high death rate. In the early stages of infection, this probably represents unsuitability of the host tissues and therefore natural immunity. The cellular reactions to malarial infection increase in intensity as the disease develops, indicating the appearance of an acquired immunity. Studies in the malaria of Central American monkeys have shown that during the initial rise of infection the phagocytosis of free merozoites and intracorpuscular parasites is sluggish. At the crisis of infection parasitized red cells, regionally concentrated in the splenic cords, are "avidly eaten". This heightened phagocytic activity represents the beginnings of acquired immunity. Once this reaction has appeared, the malarial infection is controlled and kept at a low level. Animals which have recovered from infection and are later superinfected with the same parasite exhibit very active phagocytosis immediately. Hence, although acquired immunity takes time to develop, once established, it exerts its action quickly.

Histologically, acquired immunity is characterized not only by local increase of macrophages but also by a greatly increased *rate* of phagocytosis by individual macrophages. This increased rate of phagocytosis is the specific characteristic of acquired immunity and may be related to opsonic activity of specific antibodies. The local increase of macrophages in an organ is non-specific and is not necessarily associated with acquired immunity. There may thus be a fundamental difference between the tissue response to natural and acquired immunity. This has been suggested also by the experiments of GINGRICH (1934, 1941), quoted by the author [this *Bulletin*, 1941, v. 38, 650 *bis*.]. This worker found that "blockade with foreign red cells" affected acquired but not natural immunity to *P. cathemerium* infection.

Proliferations of various tissues occur in malaria, especially in the bone marrow and spleen. In the latter there is a lymphoid hyperplasia with mitotic proliferation of the medium and large lymphocytes. Haematological changes include, according to some authors, a transient heterophil (polymorph) leucocytosis roughly contemporaneous with the segmentation of the parasites. Large mononuclears may also increase at segmentation. Reparative proliferations not immediately related to the suppression of the malarial infection also occur, *e.g.*, erythropoiesis and regeneration of liver cells. *B. G. Maegraith.*

MUKHATCHEVA, O. N. [**Fluctuation of Haemolytic and Red Blood Restoration Indices in various Stages of Malarial Paroxysms.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 34–7, 2 figs. [In Russian.]

The author describes the result of an analysis of the relationship between the destruction of red blood corpuscles, the haemoglobin content of the blood, the bone-marrow reaction, the stability of the erythrocytes and the bilirubin content of the blood in malaria. All these elements were estimated during the period covered by three paroxysms in 64 patients, whose blood was examined (1) 1–2 hours before the paroxysm, (2) at the height of the paroxysm, and (3) 24 hours after the paroxysm, the total number of examinations for each person thus being nine.

It was found that three paroxysms of malaria produced a 15–20 per cent. fall of haemoglobin content, while the number of erythrocytes was reduced by

500,000–1,000,000. The fluctuations of the red blood elements vary considerably during the different phases of the paroxysm. Sometimes there is a reduction in the number of erythrocytes and the percentage of haemoglobin during the acute period of pyrexia with a rise during the apyrexial period, while in other cases these fluctuations are absent and there may even be an increase of the indices of red blood at the height of the paroxysm. During the paroxysms, accompanied by anaemia, normoblasts (up to 4 per 100 leucocytes) appear in the peripheral blood, as well as single " irritation " cells, with poikilocytosis and anisocytosis. During the acute period of fever, there is an increase in the number of reticulocytes, which is moderate (1–2 per cent.) when the red blood indices are high, and raised (3–6 per cent.) when they are low. The increased number of reticulocytes is maintained in anaemic patients throughout all the phases of the fever. During the active period of malaria, the bilirubin content of the blood is always slightly increased, its level not being affected by repeated paroxysms. The osmotic resistance of the erythrocytes remained normal.

C. A. Hoare.

CIARAVINO, E. & SOFIA, F. Il valore della splenopuntura nelle malattie tropicali. Nota 1. Lo splenogramma nella malaria. [**The Use of Spleen Puncture in Tropical Diseases. I. The Splenogram in Malaria.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1946, v. 6, No. 5, 301–14. [Summary in English by the author.] [12 refs.]

" The value of the splenogram in tropical medicine with particular regard to diseases which show splenomegaly has been discussed by the authors.

" This first note deals with the splenogram in malaria, after a discussion about the normal splenogram in Eritrean natives.

" The essential features they have met with in malarious cases (excluding parasitological findings) are : increase of lymphoblasts ; remarkable phagocytic activity of haemohistioblastic cells ; marked erythropoietic activity and, at last, noticeable presence of free melanin and granulocytes containing melanin."

GERIN, L. La culture des quinquinas au Cameroun. [**The Cultivation of Cinchona in the Cameroons.**] *Rev. Paludisme et Méd. Trop.* 1947, Jan. 15, v. 5, No. 32, 1–9.

TRUPP, M. **Metabolism in Cerebral Malaria. (Practical and Theoretical Considerations.)** Reprinted from *Diseases of the Nervous System.* 1946, Dec., v. 7, No. 12, 8 pp. [24 refs.]

Various attempts have been made to use vasodilator or constrictor drugs in order to maintain cerebral circulation in severe malaria. The results of such experiments and of those in which oxygen has been administered have been equivocal. The author states that in a series of cases in India and Burma an oxygen-nicotinic acid regime, in addition to quinine or atabrine, was successful. The present paper attempts to rationalize this treatment. Death in cerebral malaria results because " the human encephalon is unable to sustain the following disturbances of metabolism :

1. anoxia.
2. inactivation of oxidative enzyme-substrates.
3. increased viscosity and specific gravity of the blood.
4. altered cellular permeability.
5. loss of integrity of haemato-encephalitic barrier.
6. cellular death."

The anoxic effects of malaria result from deficiency of oxygen transport due to the development of anaemia, associated with changes in the haemoglobin of the parasitized cells, and the formation of parasite pigment. Stagnant anoxia also occurs, due to " local embolic or local and general angiospastic circulatory disturbances." These circulatory disturbances give rise to intracellular oxygen defects associated with inactivation of oxidative enzyme systems. Pigment liberated from invaded erythrocytes adheres to other erythrocytes and the endothelial cells of the vessels, altering their electrical properties and so causing rouleaux " and other embolic phenomena ". This further upsets the cerebral circulation and so the cerebral metabolism. The presence of erythrocyte débris, pigment, etc., further contributes to decreased cerebral blood flow. The oxygenation upset leads to altered cellular permeability and loss of integrity of the blood brain barrier.

The author claims that nicotinic acid " aids in oxidizing the elements of toxic pigment degeneration," dissolving these from the cell surfaces, and, by improving oxidative exchange, restores cell physiological permeability and " adequate cerebral blood flow." He considers this sequence of events to be the basis of the pharmacological action of nicotinic acid in malaria. The administration of oxygen should be considered an integral part of the nicotinic acid therapy, since the combination of the two induces optimal cerebral oxygen consumption and blood flow. It is suggested also that massive destruction of available nicotinic acid occurs during the phase of " parasite multiplication ". The author therefore advises the use of nicotinic acid in all severe *P. falciparum* infections. Nicotinic acid amide may be used as a substitute.

The author suggests that both quinine and atebrin may become " encephalotoxic " (presumably by inhibition of oxidative systems) in patients in whom nicotinic acid is " paroxysmally " destroyed. " Thus it would appear that the malaria parasite invades its host seeking both respiratory pigments (hemoglobin) and its associated primary enzyme," (*sic*) " nicotinic acid ". The response of the host to such competitive activity may be complicated by the presence of the antimalarial chemotherapeutic agent, so that the introduction of " specific growth substance adjuvants " [? nicotinic acid] may be helpful to the host. Since the respiratory " avidity " of the malaria parasite is seventy times that of the normal red cell, at any rate in *P. gallinaceum* infections, oxygen administration to the host is also indicated.

Three cases treated with oxygen-nicotinic acid therapy are briefly described ; one was cerebral malaria, the other two *P. falciparum* infections with severe headache.

[The author's attempt to correlate physiological processes with the clinical picture of cerebral malaria is commendable. A good deal of the paper is, however, highly speculative and some of it both obscure and inaccurate.]

B. G. Maegraith.

Most, H., Kane, C. A., Lavietes, P. H., London, I. M., Schroeder, E. F. & Hayman, J. M. **Combined Quinine-Plasmochin Treatment of Vivax Malaria : Effect on Relapse Rate.** *Amer. J. Med. Sci.* 1946, Nov., v. 212, No. 5, 550–60, 1 chart. [13 refs.]

Seventy-two white patients with acute attacks of *P. vivax* malaria of Pacific origin were treated with quinine sulphate and plasmoquine naphthoate : 75 similar patients were treated with quinine sulphate alone, and 69 with quinacrine (mepacrine). Patients in the first group received on the first day quinine sulphate 1 gm. and plasmoquine naphthoate 0·02 gm. (0·01 gm. base) at 8-hour intervals : on days 2 to 14 inclusive, quinine sulphate 0·65 gm. and plasmoquine naphthoate 0·02 gm. were given at 8-hour intervals. The drugs

were given together. The total amount received during the 14 days was quinine sulphate 29 gm. and plasmoquine naphthoate 0·84 gm. The patients treated with quinine alone received similar doses to those above over a 14-day period. Patients in the third group each received 2·8 gm. of quinacrine during 7 days. Parasite counts were done daily until negative for 3 consecutive days. Haemoglobin, methaemoglobin and total white blood cell count determinations were made daily. After completion of treatment, the patients were transferred to a convalescent area where they were kept under observation until relapse or for a minimum of 120 days: during this period, blood smears were examined twice weekly. If parasites were found, temperatures were taken every 4 hours and daily parasite counts were made. A temperature of 100°F. or over, associated with parasitaemia, was considered a clinical relapse.

Among the 75 patients treated with quinine alone, 62 (82·8 per cent.) had a clinical relapse within 120 days; five others had a parasitaemia at some time during this period. Among the 69 patients treated with quinacrine, 56 (81 per cent.) had a clinical relapse and another two had parasitaemia. Among the 72 patients treated with quinine and plasmoquine, there were only three who had clinical relapses (4 per cent.) and five others showed parasitaemia at some time during the 120-day period.

No serious toxic manifestations were observed in 100 white patients who were given combined quinine-plasmoquine therapy for 14 days.

The authors consider that the occurrence of repeated attacks of *P. vivax* malaria at short intervals during the first six months of the disease, or repeated attacks later in the disease, is an indication for the use of combined quinine-plasmoquine treatment. Each case must be considered individually and the merits of possible cure weighed against potential toxicity. There was no evidence of serious toxicity in the authors' cases, but the patients were all white, in good physical condition, and were closely observed in hospital.

Norman White.

Brown, M. & Rennie, J. L. **Mepacrine Metabolism in Recurring Benign Tertian Malaria.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 337–46, 3 figs.

This paper deals with the metabolism of mepacrine (atebrin) in Service personnel with recurring benign tertian malaria. Plasma mepacrine concentrations during a standard course of treatment were significantly lower in patients who were suffering from relapses than in primary cases. The low plasma levels were found in those without parasitaemia or symptoms as well as in others who were undergoing an attack and were not accounted for by excessive excretion in the urine. Also there was no relation between the plasma mepacrine and the amount of drug present in the faeces. It was believed that failure of absorption may have occurred in a few cases, but plasma levels were not, in general, significantly raised when intramuscular instead of oral administration was tried. In these cases it was shown that there was no abnormal distribution of mepacrine in the various components of the blood. Observations are recorded on the changes of drug concentration in the cellular elements of blood during therapy, and it appeared that in the white cells part of the drug absorbed may be bound more firmly than the remainder and is less readily exchanged with other tissues. The sequence of events in white cells was believed to be a fair representation of what occurred in tissues. Since there was a high coefficient of correlation between plasma mepacrine concentration and that in white cells, the low plasma levels in some patients was probably not due to a high tissue concentration of the drug. The chief cause of low plasma concentration in the recurring cases of benign tertian malaria was attributed to a more rapid destruction of the drug in the body.

J. D. Fulton.

ANN. TROP. MED. & PARASIT. 1946, Dec., v. 40, Nos. 3/4, 472–81, 5 figs. [10 refs.] **Blood and Plasma Concentrations of Mepacrine in Subjects taking Suppressive and Therapeutic Dosages.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

In fasting subjects who had not previously taken the drug, 100 mgm., oral mepacrine produced a peak of plasma concentrations within four hours in most cases. In subjects on daily suppressive therapy with the same dose, the character of the plasma concentration curves remained unchanged over a period of 58 days provided the conditions of administration remained constant. This fact suggested that absorption from the alimentary tract was unimpaired during the period of observation. In the case of whole blood, the level of concentration was considerably raised at the end of the above experiment. In two groups of volunteers a daily oral dosage of 100 mgm. mepacrine gave rise to mean values in plasma concentration of 26·0 and 28·0 μgm. per litre in the case of men and women respectively, six weeks after administration was started, and these values remained fairly constant during a 10-months' course. Six weeks after treatment ended the drug was usually absent from the plasma. The mean whole-blood concentration was 150 μgm. per litre and the levels in both plasma and whole-blood varied greatly in individuals. The variations in whole-blood were considered less significant than those in plasma with regard to the suppression of malaria. During a therapeutic course of treatment in which 4·6 gm. mepacrine was given over a period of 12 days to patients with benign tertian malaria, the mean plasma concentrations ranged from 20–130 μgm. per litre. About 10 mgm. of drug was excreted daily in the urine, but in this case also there was considerable individual variation. *J. D. Fulton.*

ANN. TROP. MED. & PARASIT. 1946, Dec., v. 40, Nos. 3/4, 368–71. **The Effect of Muscular Exercise in a Hot Moist Environment on the Mepacrine Concentrations of Blood, Plasma and Urine.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

In this investigation, carried out in 1944, twenty-two volunteers receiving 0·1 gm. mepacrine (atebrin) daily over a period of several weeks, took strenuous exercise in a hot, moist chamber maintained at 32–35°C. with a humidity of 70–85 per cent., for 4 hours on 4 or 8 consecutive days, in order to see whether the plasma concentration of the drug was affected. The conditions in some respects approached those in the tropics where persons receiving suppressive treatment on similar lines were not always protected against malarial attacks. The intake of fluid, food and salt was noted, but not restricted, and each subject was weighed before entering and after leaving the chamber, in which a scheduled amount of work was performed. The urinary output while in the chamber was measured and the sweat loss calculated. Clinical observations were also made regarding temperature, pulse-rate and blood pressure. The method of MASEN [this *Bulletin*, 1945, v. 42, 8] was used to estimate minimal blood and plasma mepacrine concentrations, which are defined as "those concentrations reached on the dosage régime in question 24 hours after taking 100 mgm. (*i.e.*, immediately prior to a dose)". Further estimations were made at various times. The urinary mepacrine excretion over 24 hours was also measured in conjunction with them. The exercise in the hot chamber did not affect minimal levels of the drug in blood and plasma. There was an increase in urinary mepacrine excretion while in the chamber, and this is believed to be associated with increased excretion of ammonia. *J. D. Fulton.*

ANN. TROP. MED. & PARASIT. 1946, Dec., v. 40, Nos. 3/4, 482–92, 6 figs. **The Effect of various Substances, including Food, on the Absorption of orally administered Mepacrine Hydrochloride.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

In this investigation an answer was sought to the question whether the presence of food in the stomach interfered with the absorption of mepacrine given orally. In carefully controlled experiments, it was found that the final plasma levels of the drug during a course of treatment showed no significant variation whether the drug was given on a full or empty stomach. However, when food was present, the rate of absorption at the start may have been slightly decreased. Urinary output of mepacrine for each 24-hours period during treatment was significantly less in the case of those who received the drug on a full stomach, but after treatment was completed the output of the two groups by this route became less unequal. Large amounts of cellulose in the diet, and the taking of kaolin, magnesium trisilicate or McLean's powder, which readily adsorb the drug *in vitro*, did not affect absorption from the gut. They may, therefore, be taken by subjects receiving suppressive mepacrine without affecting to any extent the plasma levels attained. *J. D. Fulton.*

ANN. TROP. MED. & PARASIT. 1946, Dec., v. 40, Nos. 3/4, 372–9. **The Excretion of Mepacrine in the Faeces.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

The faecal excretion of mepacrine has been measured at various times in persons receiving 0·1 gm. of the drug daily for different periods. On this dosage over a period up to six months the excretion was not significantly altered. There was great variation in individual excretion, in some cases up to 30 per cent. of the administered dose being eliminated by the bowel. The amount excreted in the bile was previously found to be small, but when the drug was given intramuscularly to a number of subjects, the faecal output was considerable. Elimination of mepacrine by the bowel therefore does not depend on failure of absorption. There was no relationship between the amount excreted in the faeces and the levels of mepacrine in the blood of plasma, or in the urine.

The results of experiments in rats were in agreement with those obtained with human subjects in that no significant increase in faecal mepacrine occurred when the drug was administered over long periods. The value of two different procedures for the estimation of mepacrine in faeces is discussed, and, as before, MASEN's method [this *Bulletin*, 1945, v. 42, 8] was employed in the determinations. It was found that mepacrine hydrochloride was stable in faecal suspensions at room temperature for a period of at least three days.

J. D. Fulton.

KIERLAND, R. R. **Drug Eruption due to Atabrine and resembling Lichen Planus.** *Proc. Staff Meetings Mayo Clinic.* 1946, Oct. 16, v. 21, No. 21, 404–8.

This report is based on a study of 49 cases. The first appearance of the lesions was usually within 3–6 months after the patients commenced to take mepacrine. When the drug was discontinued, the eruption remained stationary for a variable period and then retrogressed. Pigmentation persisted for months.

The author describes briefly the signs and symptoms which have been referred to in this *Bulletin* on several occasions [1946, v. 43, 301, 303 *bis*; 1947, v. 44, 33].

He noted that the eruption almost invariably occurred in the higher age groups of the population at risk.

The results of routine analysis of blood and urine were within normal limits except when clinical complications existed. Bacteriological studies of individual lesions were made in ten cases. Neither fungi nor spirochaetes were found in the lesions. In 39 cases, patch-tests for sensitivity to mepacrine were made; the results were negative.

The most serious complication was aplastic anaemia; death occurred in all cases in which this developed.

Histopathological investigation showed that "the eruption due to atebrine starts out with histologic changes closely resembling ordinary lichen planus; namely, increase of the *stratum granulosum*, liquefactive degeneration of the basal layer, moderate acanthosis and a cellular infiltrate usually limited to the upper portion of the cutis. Keratotic plugging of the dermal appendages is a feature of the verrucous and hypertrophic lesions as well as of the lesions which simulate those of lichen spinulosus or of lichen pilaris seu spinulosus. The infiltrate may extend deep in the cutis when the lesions in the drug eruption simulate those in lichen spinulosis or in lichen pilaris seu spinulosus. In the more severe types of involvement destruction of the sebaceous glands and later atrophy and destruction of the hair follicle occur, but usually the arrectores pilorum muscle is preserved. Sweat glands may also be destroyed by the infiltrate. In patients who clinically have primary or secondary eczematous features, histologic evidence of eczema is found also.

By the use of special stains for the microscopic examination it was determined that the pigment is melanin; the increase in pigmentation may be marked unless acanthosis is severe. On occasion, the acanthosis is so extreme that the changes may be represented as pseudo-epitheliomatous. Unless the cellular infiltrate is dense, elastic tissue is not changed much.

No new measures for treatment have been discovered.

The author states categorically that the eruption is due to mepacrine.

R. M. B. MacKenna.

LUM, L. C. **Fatal Hepatitis associated with Tropical Lichenoid Dermatitis.** *Med. J. Australia.* 1946, Dec. 21, v. 2, No. 25, 866–8.

"A case of fatal acute hepatitis associated with tropical lichenoid dermatitis is described. It is suggested that the simultaneous onset of the two conditions may indicate a common aetiology."

GAGE, J. C. & ROSE, F. L. **The Estimation of Paludrine in Urine.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 333–6, 1 chart.

A method is described for the rapid estimation of Paludrine in urine which is more specific but lacks the sensitivity of that previously described by SPINKS and TOTTEY [this *Bulletin*, 1946, v. 43, 400, 707]. It is, however, more easily carried out and may be used in field investigations when absorption and excretion of the drug are being studied. It depends on the fact that Paludrine forms a purple copper complex in which two molecules of the base are associated with one atom of the metal and a molecule of water [CURD & ROSE, this *Bulletin*, 1947, v. 44, 283]. This complex is unstable in the presence of acids but more so in the presence of alkalis and while insoluble in water it dissolves in organic solvents such as benzene, xylene and chloroform. When its solution in an organic solvent is shaken with sodium diethyldithiocarbamate in water the characteristic colour with copper is produced, proportional in intensity to the amount of metal present. By this means, Paludrine can be satisfactorily estimated in urine containing 5 to 100 mgm. per litre. The test is carried out by

mixing 2 ml. of urine in a test tube with 1 ml. of an aqueous copper sulphate-ammonium chloride solution and 1 ml. normal caustic soda. After a few minutes the tube is shaken with 5 ml. benzene, the benzene layer is then removed, washed with 1 ml. water and shaken with 1 ml. of 0·1 per cent. aqueous solution of the reagent for 1 minute. The intensity of the golden-yellow colour produced in the benzene is measured, preferably in a Spekker absorptiometer, with the aid of suitable filters, and the amount of Paludrine present determined by comparison with a standard curve similarly constructed. The reaction appears to be a general one for mono- and dialkyl substituted *p*-chlorophenylbiguanides, but not for their probable metabolic products. Lower results are therefore obtained than by the method previously described. *J. D. Fulton.*

MAEGRAITH, B. G., TOTTEY, Mary M., ADAMS, A. R. D., ANDREWS, W. H. H. & KING, J. D. **The Absorption and Excretion of Paludrine in the Human Subject.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 493–506, 4 figs. [25 refs.]

The absorption and excretion of Paludrine and its distribution in the cellular elements of the blood has been investigated in normal persons and in those infected with benign or malignant tertian malaria. The authors are of the opinion that the suppressive and therapeutic activity of the drug are related to its plasma concentration.

In the present experiments paludrine was given orally as tablets and also intravenously. Estimations were made by the method of SPINKS & TOTTEY [this *Bulletin*, 1946, v. 43, 707] on fresh specimens or in those kept in the cold, although in faeces the drug proved stable under various storage conditions. Plasma concentration curves after various single oral dosages were constructed and a peak of concentration was found to be reached approximately 4 hours after dosage. The usual individual variations were noted. During therapeutic courses of 500 mgm. and 50 mgm. given every 12 hours over a period of 14 days, estimations of plasma concentration were made just prior to the next dose. Levels up to 500 and 150 μgm. per litre respectively were attained on the larger and smaller doses, the peak values being reached more rapidly than in the case of mepacrine, a point which may be of practical significance. One week after administration ceased, the drug was no longer detectable. In doses up to 50 mgm. given intravenously, no toxic signs were noted and there was a rapid fall from the peak value in the plasma. In one experiment the ratio of whole blood to plasma concentration was about 3.

At two autopsies it was found that the greatest concentration of the drug was present in kidney and next in the liver. The concentration of the drug in a white cell of the blood was estimated to be 50 to 120 times that in an erythrocyte, a ratio which is smaller than in the case of mepacrine. In solution in plasma, about 75 per cent. of the drug appeared to be bound to protein. After single doses, about 40–60 per cent. was excreted in the urine and 10 per cent. in the stools. On the above therapeutic doses of 500 and 50 mgm. twice daily over 14 days, the drug was detectable in urine for 9 and 6 days respectively.

J. D. Fulton.

FINDLAY, G. M., MAEGRAITH, B. G., MARKSON, J. L. & HOLDEN, J. R. **Investigations in the Chemotherapy of Malaria in West Africa. V. Sulphonamide Compounds.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 358–67.

This investigation, carried out during the late war and, for security reasons, not previously reported, deals with the treatment of malignant tertian malaria

in Europeans in W. Africa. Six sulphonamides and a Schiff's derivative from a sulphonated diaminodiphenyl sulphone were used in the treatment of 136 patients. The total dosage over a period of six days was 108 gm. in the case of succinylsulphathiazole, 26 gm. for the other sulphonamides and 25 gm. for the Schiff's derivative. Parasites were present in the blood when treatment was begun and the results obtained were compared with those for patients under similar conditions who received treatment with quinine or mepacrine. Duration of fever and parasitaemia were used as criteria of therapeutic effect. The following is the author's summary :—

" The therapeutic effect of certain sulphonamide drugs has been investigated in cases of malignant tertian malaria in European troops in West Africa.

" Sulphadiazine, sulphathiazole, sulphamezathine and sulphamerazine had a slight effect in controlling infections, but were far inferior to mepacrine and quinine.

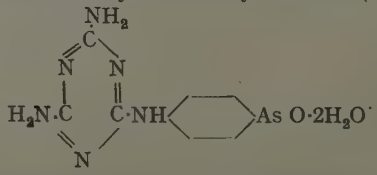
" Sulphapyrazine and succinylsulphathiazole were of little value. Nineteen of 25 cases treated with sulphamezathine showed gametocytes in the blood films. There is some evidence that such gametocytes are incapable of infecting *A. gambiae* mosquitoes."

J. D. Fulton.

PAYNE, E. H., BALTHAZAR, E. & BEZERRA, D. A. **Preliminary Observations on the Use of Melarsen Oxide in Malaria.** *Southern Med. J.* 1946, Dec., v. 39, No. 12, 970–72.

——, —— & FERNANDES, J. S. **Further Experience with Melarsen Oxide (a New Arsenical) in the Treatment of Tropical Disease.** *Ibid.* 972–5.

WEINMAN & FRANZ [this *Bulletin*, 1946, v. 43, 207] found melarsen oxide, which is the stable crystalline dihydrate of 2-(4'arsenosoanilino)-4,6 diamino-s-triazine,



to be effective in limited trials of African trypanosomiasis. Some benefits from its use in human filariasis were noted by ROSE & CULBERTSON (*J. Parasitology*, 1945, v. 31, Suppl. p. 17).

i. The present authors have used it in the treatment of 58 cases of acute and chronic malaria (type not always determined) in patients suffering from other diseases. The general course of treatment was 7 intravenous injections of 25 mgm. which was tolerated without signs of toxicity. Symptoms of malaria subsided on the 4th or 5th day and there was general improvement in the clinical condition.

ii. Other tropical diseases were treated in the district of Minas Gerais and Goias, Brazil, with doses of 25 to 75 mgm. daily for several days. In tropical ulcer, favourable results were obtained with relatively rapid healing. In 35 cases of secondary yaws, there was also rapid response to the drug and the results compared favourably with those obtained by mapharsen.

J. D. Fulton.

GOLDSMITH, K. **A Controlled Field Trial of SN 7618-5 (Chloroquine) for the Suppression of Malaria.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 311–16.

At the request of the U.S. Army Medical Authorities, a test was carried out in August–November 1945 to determine the value of SN 7618-5 (Winthrop

Chemical Co., Inc., Rensselaer, N.Y.). The labourers selected for the trial were living in an isolated group of quarters on a tea estate, where malaria is hyperendemic, in north-east Assam. *A. minimus* is the vector. During the experiment, all anti-larval and anti-adult mosquito measures were discontinued. The drug was given in tablet form : each tablet contained 0·48 gm., 0·3 gm. of base. The dose recommended as a suppressive was one tablet a week.

The subjects were divided into 3 groups : 76 were controls ; 74 received one tablet of atebrin daily ; 73 received one tablet of SN 7618-5 each week. Weekly blood examinations were made until the end of the experiment. In the eighth week, the control group were given SN 7618-5 ; the administration of this drug to the two groups was continued till the 14th week. The atebrin group ceased taking the drug in the eighth week. A similar experiment was with three groups of 12 children each, from 6 to 14 years of age ; the dosage was made halved.

From the fourth week, there was a sharp rise in the parasite rate of the controls and a significant fall in the parasite rates of the atebrin and SN 7618-5 groups, amounting to complete disappearance in the latter. The few cases of " break-through " in the atebrin group may have been due to irregularities in taking the drug. There were a few cases of intolerance to atebrin, none to SN 7618-5 ; there were a few pregnant women in the latter group. Children tolerated both drugs well. The large bulk of the SN 7618-5 tablets was the sole inconvenience, especially when they were given to children. On some occasions, SN 7618-5 was given on an empty stomach without any ill effects.

Norman White.

BANG, F. B., HAIRSTON, N. G., MAIER, J. & TRAGER, W. **Studies on Atabrine Suppression of Malaria. II. An Evaluation of Atabrine Suppression in the Field.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 753–9, 2 figs.

To determine the value of a drug as a suppressive of malaria it is necessary to have information as to the expected attack rate were suppression not in force. Such information is often unobtainable in field conditions, but by careful parasite surveys of troops, some of the factors in operation may be determined. Men of a highly infected group under rigidly supervised atebrin suppression, who had not had a clinical attack of malaria for some weeks, were examined ; parasites were found in 14 per cent. The transient parasitaemia was unrelated to atebrin levels. These men had had only few previous attacks of malaria. In comparable groups of men who had had much previous clinical malaria, the number of positive smears was very small, 2 out of 349. Very rarely does the parasite density in individuals on adequate atebrin suppression exceed 5 per 500 white blood cells.

A careful study was made of a regiment who had been in severe jungle combat for two months in the Buna campaign. Careful history taking, determination of atebrin levels and the examination of blood smears led to the conclusion that at least 98 per cent. of the men in strenuous combat were protected by 1·0 gm. of atebrin a week. This was usually taken in two doses of 0·5 gm. each.

Norman White.

MARIKOVSKI, P. I. [**Attempt in the Use of the Energy of Gunpowder Gases for spraying Insecticide Powders.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 55–8, 2 figs. [In Russian.]

The author describes a method of spraying insecticide powders, such as pyrethrum, with the help of a special rocket pistol. This has a barrel 150 mm. long with a bore 26 mm. in diameter. To the end of the barrel is attached a

funnel-shaped tin extension 30 cm. long. A cartridge 10 cm. long is filled with 0·5 gm. of black gunpowder and plugged, after which pyrethrum is introduced into the funnel in a quantity varying with the size of the room to be treated (2 gm. per 1 sq. metre). When the pistol is fired, a cloud of pyrethrum hits the ceiling and is dispersed through the room. In this way it is possible to kill all the mosquitoes present in 10–15 minutes. This pistol can also be used for dusting mosquito breeding places with Paris green. *C. A. Hoare.*

British Guiana. **Malaria Research Service. Medical Department. Progress Report for the Half Year January–June, 1946** [Giglioli, G., Hon. Govt. Malariologist]. 10 mimeographed pp., 2 plans.

Preliminary trials of DDT residual spraying of houses in British Guiana carried out in 1945 were described in a previous report [this *Bulletin*, 1947, v. 44, 181]. The present report describes the considerable extension of the work during the first half of 1946, when 2,711 buildings containing 9,222 rooms were treated. The population under DDT protection was 16,000, excluding some 4,000 inhabitants of a ward in the City who have been similarly protected since August 1945. The 1946 observations confirm the encouraging results of the previous year. The long-lasting effect of DDT residual spraying on the house-haunting mosquitoes *Anopheles darlingi* and *Aëdes aegypti* were marked; *Culex fatigans* was more resistant.

With the cooperation of the Sugar Industry and the Yellow Fever Service, the Malaria Research Service now propose a much extended area of operation including the Demerara River Estuary (population 35,589) and the Berbice River Estuary (population of malarious sections about 10,000). Such a large-scale experiment should yield unequivocal conclusions as to the value of this mosquito and malaria control method and permit the formulation of a definite control policy. *Norman White.*

Jones, H. A., Incho, H. H. & Deonier, C. C. **Comparative Toxicity of *p,p'*- and *o,p'*-DDT to Larvae of** *Anopheles quadrimaculatus*. *J. Econom. Entom.* 1946, Oct., v. 39, No. 5, 672–3, 1 fig.

The *ortho-para'* isomer is one of major impurities in commercial DDT and this is known to be much less toxic to most insects than the active *para-para'* compound. Tests were made with pure o,p'-DDT and pure p,p'-DDT and mixtures of them in different proportions, to larvae of *Anopheles quadrimaculatus*.

From the median lethal concentrations, the p,p'-DDT appears to be six times as toxic as the o,p'-DDT to these larvae. Relationship of toxicity to the proportion of p,p'-DDT in a mixture is curvilinear; proportions above 25 per cent. have a rather greater effect in increasing insecticidal power than would be expected. *J. R. Busvine.*

Zuckerman, A. **Infections with** *Plasmodium gallinaceum* **in Chick Embryos induced by Exoerythrocytic and Blood Stages.** *J. Infect. Dis.* 1946, July–Aug., v. 79, No. 1, 1–11, 15 coloured figs. on 1 pl. [18 refs.]

After a brief review of the literature dealing with the infection of avian embryos with malaria by inoculation with avian malarial parasites the author gives an account of his own investigations with *P. gallinaceum*. Infections were induced in two ways. Firstly, emulsions of brain containing exoerythrocytic as well as erythrocytic stages were implanted on to the chorio-allantoic membrane

of the embryos from the 4th to the 14th day of development. Secondly, blood containing erythrocytic stages was inoculated into embryos intramuscularly.

By the first method, when the brain emulsion had been successfully fixed to the membrane by plasma clot and the embryo had survived to the 6th day following the operation, infection invariably resulted. Though erythrocytic and exoerythrocytic forms appeared in the embryos simultaneously, the latter predominated. The highest erythrocytic infection recorded involved only 22 per cent. of the red cells. The number of exoerythrocytic stages, on the other hand, often far exceeded the number usually found in three-weeks-old chicks after sporozoite infection. In the embryos they were found in monocytes, macrophages, myelocytes, capillary endothelium or they were lying free in the capillary lumen or amongst tissue cells. In one embryo they were abundant in the circulating blood within leucocytes of every kind and also in all cells of the erythrocyte series, as occurs regularly in *P. elongatum* infections. This embryo exhibited the *P. mexicanum* type of infection of THOMPSON and HUFF. In a coloured plate the appearance of these infected blood cells is shown.

When the second method of infection was adopted by inoculating blood intramuscularly, the result was quite different and, in the case of embryos which lived long enough, resembled the similarly produced infection in adult fowls. There was heavy erythrocytic infection with only a few exoerythrocytic stages. It is noteworthy that when attempts to produce infection by fixing to the chorio-allantoic membrane blood clot containing erythrocytic stages in place of brain emulsion, infection did not occur. This appears to indicate that the infection through the membrane was brought about exclusively by the implanted exoerythrocytic stages.

Testing *in vitro* cultures of spleens from infected embryos by Hawking's tissue culture method, it was found that a more extensive growth of exoerythrocytic stages occurred than when adult spleens were used. By exposing exoerythrocytic forms in embryonic spleen material to the action of drugs before planting in tissue culture medium, the possible therapeutic effect of such drugs can be tested. Similarly by treating brain emulsion with drugs before implanting it on the chorio-allantoic membrane, the effect of these drugs can be gauged. Quinine, atebrin and plasmochin were each tested on two embryos. Neither of the first two had any action, but in the case of plasmochin there was a definite suppressive effect on one embryo as the development of exoerythrocytic forms was at least 20 times lower than in the control. In the other embryo, no suppressive action was noted. Sulphadiazine had a marked suppressive effect on the stages in brain emulsion as judged by the degree of subsequent infection in embryos. *C. M. Wenyon.*

RIGDON, R. H. & VARNADOE, Nona B. **Effect of Oxygen on Malaria. An in Vivo Study in Ducks.** *J. Lab. & Clin. Med.* 1947, Jan., v. 32, No. 1, 57–65, 5 figs. [11 refs.]

"Ducks with a severe malarial infection when placed in an oxygen chamber immediately show marked clinical improvement. They survive for ten to eighteen hours longer than similarly infected ducks kept in the duck room. This improvement is attributed to the greater amount of oxygen available for transmission to the anoxemic tissues.

"The use of oxygen in the treatment of acute malarial infections in man is discussed."

BLACKWATER FEVER.

ABBOTT, P. H. **A Case of Blackwater Fever during Mepacrine Therapy.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 354–6.

A European woman, aged 34, in an area of hyperendemic malaria in the Sudan, developed a typical attack of blackwater fever while undergoing mepacrine treatment. She had been given 0·3 gm. a day for five days and then 0·1 gm. daily. The symptoms of blackwater fever developed when she had taken in all 2·7 gm. of mepacrine and one would have expected the blood concentration of mepacrine to have been sufficiently high to afford protection from blackwater fever. *Norman White.*

DA FONSECA SANTOS, H. S. A febre biliosa hemoglobinúrica na região de Camacupa. [**Blackwater Fever in the Camacupa District.**] *Africa Méd.* Lisbon. 1946, Sept.–Oct., v. 12, Nos. 9/10, 153–80, 6 graphs & 2 figs.

The author, who was Health Delegate to Camacupa in October 1943, and observed that cases of blackwater fever were unexpectedly numerous [but the annual average appears to have been only nine], examined the statistics for the years 1937 to 1943 and found that the highest incidence of the disease was in May and June, 20 and 24·6 per cent. respectively, but low, 1·6 per cent., in January, August, September and December [with so small a total these percentage figures lose much of their apparent significance]. Males were twice as often attacked as females, and whites twice as often as half-castes and blacks together. Three cases are detailed: one, in a man of 20 years, a mild attack, with recovery; another, age not stated, severe attack but apyrexial, also recovered; the third, in a man of 25 years with remittent fever up to 40·8°C., becoming normal 10 days after admission. All were whites.

The author gives in a table 23 " medicaments " in common use in this disease [many of these are purely for symptomatic treatment, such as champagne as a stimulant and diuretic, tonics in convalescence, campolon for the anaemia, etc.]. He then details his own method of treatment, but doses are given in some instances only.

The treatment, which is shown in detail for three days, includes a formidable list of drugs and remedies, and is somewhat heroic. [Nevertheless, as the cases detailed show, recovery took place.] *H. Harold Scott.*

TRYPANOSOMIASIS.

FAIRBAIRN, H. & BURTT, E. **The Infectivity to Man of a Strain of *Trypanosoma rhodesiense* transmitted cyclically by *Glossina morsitans* through Sheep and Antelope: Evidence that Man requires a Minimum Infective Dose of Metacyclic Trypanosomes.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 270–313, 3 figs. [49 refs.]

This paper was written to report tests of the infectivity to man during the years 1940–45 of a strain of *Trypanosoma rhodesiense* which was isolated in 1934 by the abstracter and has since been maintained by cyclical transmission by *Glossina morsitans*, mainly through sheep and antelopes. The authors' headings are used in the abstract.

The infectivity to man of a strain of T. rhodesiense.—The strain was cyclically transmitted through several series of animals—the " sheep line ", " M/1 sheep

line", "monkey line", "impala line", "Thomson's gazelle line" and others—tests of infectivity being made on volunteers from time to time, while observations on its transmissibility by *G. morsitans*, and its infectivity and virulence to white rats and other animals were also made. The authors found "that the strain of *T. rhodesiense*, taken as a whole, was still highly infective to man 10½ years after isolation, and that it showed no signs of reverting to *T. brucei*, as Yorke *et al.*, postulated would happen." The resistance of the strain to human serum had been tested in 1936 and 1938 and found to be undiminished.

The failure of man to be infected.—Volunteers who had resisted infection from the bites of isolated infective *G. morsitans* were re-bitten by the same fly, or by another fly which had fed on the same infected animal, or by a fly which had fed on another animal infected with this strain. In the case of the same fly, 12 out of 35 men became infected, 4 out of 13 were infected by another fly of the same "isolation", 6 out of 14 by a fly from a different isolation from the same animal host, and 7 out of 18 by a fly from a different animal host. The authors attribute these results to variations in the dose of trypanosomes injected by the flies, though differences in resistance among the men also played a part.

An interesting observation was the recovery from infection of three monkeys (*Cercopithecus* sp.), a very susceptible species in which infection is nearly always fatal; in other monkeys, cyclically infected from these three, the strain showed no decrease of its usual virulence. As these three monkeys were infected yet developed a successful resistance, the authors conclude that it may be possible to immunize people and that this should be investigated.

The minimum infective dose of metacyclic trypanosomes required to infect man.—BURTT [this *Bulletin*, 1946, v. 43, 1121] counted the numbers of trypanosomes ejected on to glass slides by the fly when attempting to feed and found that the numbers varied greatly at different attempts by the same fly and with different flies. From these observations and from the tests on volunteers the authors conclude that the minimal infective dose for man of the fly's gland trypanosomes of this strain is about 350. Fairbairn also counted the living trypanosomes ejected by flies and then inoculated them into volunteers; of 19 men so inoculated, 15 were not infected by 88, 111, 128, 143, 146, 177, 188, 206, 220, 308, 362, 680, 800, 833, and 1,067 trypanosomes respectively, while 4 men were infected by 170, 284, 389, and 455 trypanosomes respectively.

The authors give examples of experiments supporting their view of the importance of the dose of trypanosomes. They suggest that the ability of a fly to inoculate an infective dose depends on at least two factors: (*a*) the power of the trypanosomes to invade the salivary glands (transmissibility) and (*b*) the ability of the trypanosomes to multiply in the glands. The virulence of the strain may also be a factor, for the minimal infective dose may be smaller in a virulent line than in a less virulent one.

Factors influencing the transmissibility and dosage of the strain.—There was a correlation between transmissibility and infectivity of the three lines maintained in sheep, Thomson's gazelle, and monkey respectively. Higher transmissibility rates were obtained from some species of animals than from others, but in transfers from one species to another, both transmissibility and dosage were found to increase or decrease together. Transmissibility was also affected by atmospheric temperature; BURTT [this *Bulletin*, 1946, v. 43, 827] incubated pupae of *G. morsitans* and found that transmissibility was increased in the hatched-out flies, that the cycle of development of the trypanosomes in the flies was shortened, and that the viability of the flies was apparently increased. The possible practical importance of this in nature is pointed out.

The virulence of the strain.—This was judged by the length of life of infected animals, especially rats; as the length of life of sheep and monkeys was found to be closely parallel to that of rats, the latter could be used as an index of the

former. Variations in virulence are described in detail; infectivity and virulence (in the sheep, Thomson's gazelle and monkey lines) during a period of a few years did not vary similarly, and the authors conclude that "infectivity to man is not bound up with the virulence of the trypanosome and that virulence and infectivity to man are two separate and independent variable qualities of a trypanosome."

The infection of rats from man.—Great differences in infectivity were found between the different "lines" when rats were inoculated from infected men; with the main sheep line inoculation often failed to infect the rats and the course of the infection in the infected rats was often chronic and relapsing, with few posterior-nuclear forms. The authors think that this was due to an actual change in the trypanosomes caused by prolonged residence in sheep. Inoculated rats lived longer than fly-infected rats [noted also by the abstracter, this *Bulletin*, 1939, v. 36, 210].

The atypical infections of man with T. rhodesiense.—The cases of 4 volunteers with very chronic infections are described; all were infected from the sheep line. Another interesting result was obtained with two flies which had fed on an infected man at the same time; one fly infected 3 out of 10 men, causing acute infections, while the other fly, which ejected very few trypanosomes in slide tests, infected 1 out of 3 men, causing a very chronic infection with unusual local reactions.

Discussion.—The authors criticize Duke's results and views, applying their theory of the importance of the dose of trypanosomes which, they think, offers a different explanation of those results and leads to somewhat different conclusions.

Their results with incubated pupae make a reconsideration of much former work desirable.

They suggest that alterations in virulence in the various "lines" of the strain were due to gene mutation.

Finally they refer to HOARE's paper on biological races among protozoa [this *Bulletin*, 1944, v. 41, 150].

[This paper contains a large amount of interesting detail set out in tables and charts as well as in the text; it will, no doubt, be read in the original and closely studied by all who are interested in trypanosomiasis. The emphasis laid by the authors on the infective dose of trypanosomes may not be accepted unreservedly by some workers; the abstracter's suggestion of the probable importance of selection acting on a heterogeneous strain is published in his papers on the experiments at Tinde before 1939, and in this *Bulletin*, 1946, v. 43, 169.] *J. F. Corson.*

SCHWETZ, J. Sur la cause directe de la répartition des diverses espèces de tsétsés dans la même région. [**The Causal Distribution of different Species of Tsetse Flies in the same Region.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 9/10, 367–72.

The author repeats the familiar observation that in West Africa, species of Glossina show a well-defined zonation. For instance in the Ivory Coast one finds *G. pallicera*, *fusca* and *nigrofusca* in equatorial forest near the coast. Further north these cease to occur: in the savanna with water-side strips of forest *G. tachinoides* and *submorsitans* replace them. *G. palpalis* is widely distributed in nearly the whole area, but in the north is strictly limited to dense thicket, generally beside water. The author cannot feel convinced that this distribution is due either to climate or to the distribution of plants. He feels that too little weight has been allowed to the "law of geographical distribution"

under which a species occurs in one area, but not in another which appears to be suitable.

The paper contains some useful facts about the localities in which certain rare species, *tabaniformis*, *schwetzi*, *newsteadi* and others have been captured.

P. A. Buxton.

HENDERSON-BEGG, A. **Heterophile Antibodies in Trypanosomiasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 331–9. [18 refs.]

A heterophile reaction is defined as that type of reaction which occurs between an antigen and an antibody unrelated in their origin. The production of heterophile antibodies in man has been demonstrated after the injection of horse serum and in cases of infective mononucleosis, their presence in the latter instance being considered of diagnostic significance. The purpose of the present paper is to describe the finding of heterophile agglutinins, in relatively high titre, in cases of human trypanosomiasis examined in West Africa.

Among 100 proved cases of infection with *T. gambiense* at least 30 per cent. gave an agglutination titre significantly higher than the control level, which was represented by similar tests carried out on the sera of 100 individuals who were either normal or else suffering from diseases other than trypanosomiasis. In view of these findings it is suggested that "care must be taken before a diagnosis of infective mononucleosis is made in the tropics, or in patients recently returned from the tropics."

Although the reaction may be non-specific, absorption tests carried out by the author suggest that the antibodies demonstrated in the serum of patients suffering from trypanosomiasis are in certain respects unique. Thus the antibody present in trypanosomiasis is absorbed by guineapig kidney whereas that present in infective mononucleosis is not. On the other hand, the differentiation of the trypanosomiasis agglutinins from those present in serum sickness is less clear, as in both cases there is a considerable degree of absorption with beef cells as well as with guineapig kidney.

R. M. Gordon.

LAUNOY, L. & PRIEUR, M., Mlle. Sur l'action trypanocide spéciale de certains dérivés de la phénanthridine pour *T. congolense*. [**The Special Trypanocidal Action of certain Phenanthridinium Compounds for** *Trypanosoma congolense*.] *Ann. Inst. Pasteur.* 1947, Jan., v. 73, No. 1, 58–64.

The authors refer to the two compounds: 7-amino-9 (*p*-aminophenyl)-10 methylphenanthridinium chloride (compound S.897), and 2 : 7-diamino-10 methylphenanthridinium bromide (compound S.1553), elaborated by BROWNING and his collaborators [this *Bulletin*, 1938, v. 35, 344; 1945, v. 42, 258, 259], and tested in Uganda by CARMICHAEL and BELL [*ibid.*, 1945, v. 42, 259, 260] on cattle infected with *T. congolense*. A third compound, with $-O.SO_2OH$ in place of the Br of S.1553, was also studied in the same way; this is called the acid sulphate compound. In their own experiments, the present authors tested the drugs on mice, rats and (in some cases) guineapigs, infected with *T. brucei*. *T. congolense*, *T. evansi*, *T. annamense* (a chemo-resistant strain) or *T. equiperdum*. The results are set out in detail, and those interested in the minutiae of dosage and effects should consult the original paper.

In general, the compounds were active only against *T. congolense*, though they had some effect on *T. brucei* in the rat. The following table, constructed from the authors' figures, gives an idea of the toxicity of the drugs for mice, and of their effect on *T. congolense* infections in mice :—

	897	1553	Acid sulphate compound
Toxic dose for mice (LD50):			
Intravenous	0·35 mgm.	0·75 mgm.	0·7 mgm. (LD40)
Subcutaneous	1·5 mgm.	1·0 mgm.	1·5 mgm. (LD66)
Sterilization of *T. congolense* infection:			
Intravenous	0·075 mgm.	0·25 mgm.	0·025 mgm.
Subcutaneous	0·1 mgm.	0·075 mgm.	0·075 mgm. (variable)

It is evident that these drugs are valuable agents for the cure of *T. congolense* infections, as had already been indicated by the work of Carmichael and Bell. They can be injected subcutaneously, and this route is sometimes more efficacious than the intravenous route. None of them has any preventive action against any of the trypanosomes studied. *Charles Wilcocks.*

SERRA, G. Il problema della tripanosi umana ed animale in A.O.I. [**The Problem of Human and Animal Trypanosomiasis in Italian East Africa.**] *Attualità Med.* Rome. 1940, July–Oct., v. 5, Nos. 7/10, 117–24.

ANGEL TORRICO M., R. Nuevos reservorios domesticos de *Schizotrypanum cruzi.* [**New Domestic Reservoir Hosts of** *Trypanosoma cruzi.*] *An. Laboratorio Central.* Cochabamba, Bolivia. 1946, July, v. 1, No. 1, 11–19, 2 figs.

The author names 35 vertebrate hosts of *T. cruzi*, exclusive of man, given in a list by TALICE in his book the *Parasitic Diseases of Man.* When on a visit to Cochabamba, the author entered a poor dwelling and caught 364 specimens of *T. infestans* in different stages of growth and found, on examination of their faeces, 194 (53·2 per cent.) positive. Eight of the persons living there were examined but none showed any sign of infection. They kept guineapigs, as many of the people do, breeding them for the table, and examination of these animals proved them to be heavily infected. Triatomata and guineapigs obtained from other dwellings confirmed these findings. *H. Harold Scott.*

ANGEL TORRICO M., R. Hallazgo de *Eratyrus mucronatus*, infestación natural de "Vinchucas" de cerro y *Eutriatoma sordida* en Cochabamba. [*Eratyrus mucronatus* **and** *Eutriatoma sordida* **in Cochabamba. Natural Infestation of Bugs in the Hilly District.**] *An. Laboratorio Central.* Cochabamba, Bolivia. 1946, July, v. 1, No. 1, 19–23, 3 figs. [10 refs.]

The author gives a list of seven commonly known vectors of *T. cruzi* in Bolivia, namely, *T. infestans, Eutriatoma sordida, E. oswaldoi, E. venosa, Rhodnius pictipes, Panstrongylus geniculatus* and *Psammolestes coreodes.*

Examining for these in Magdalena district of Beni the author came across large numbers of *E. sordida*, many of them infested, and also a new species of Triatoma, *Eratyrus mucronatus.* This brings the Bolivian species of Triatomas up to eight in number. He examined several of them but, although they were living together with the infected *E. sordida*, he could not find any infected among them. *H. Harold Scott.*

D'ANDURAIN, C. W. Observaciones histopatologicas de *Octodon degus* naturalmente infestados con *Trypanosoma cruzi*. [**Histopathological Observations of *Octodon degus*, naturally infected with *T. cruzi*.**] *Biológica*. Santiago. 1945, Dec., No. 3, 93–106, 12 figs. [Summary in English by the author.]

"The author communicates the results of a research work on parasite reservoirs of Chagas Disease, carried out in the surroundings of the Mines of Altamira, Domeyko (Province of Atacama, Department of Vallenar Par. 28°50′). These results consist in the finding of three specimens of *Octodon degus degus* Molina, naturally infested with *Trypanosoma cruzi*, out of 12 specimens examined, and from a total lot of 402 mammals captured. The finding was made by means of xenodiagnosis, and was later confirmed through the discovery of leishmanoid forms of the parasites in the tissue of these rodents.

"The histopathological examination of the lesions shows that they do not differ essentially from those observed in laboratory animals experimentally infected with the parasite. In one of the specimens examined, a nest of flagellate forms of the *T. cruzi* was found imbedded in a cardiac muscular fibre."

PIZZI P., T. Algunos aspectos de la enfermedad de Chagas experimental. Comunicación preliminar. [**Some Experimental Aspects of Chagas's Disease. Preliminary Report.**] *Biológica*. Santiago. 1945, Dec., No. 3, 53–68, 15 figs. [10 refs.] English summary.

BADÍNEZ S., O. Contribución a la anatomia patologica de la enfermedad de Chagas experimental. [**Observations on the Pathological Anatomy of Experimental Chagas's Disease.**] *Biológica*. Santiago. 1945, Dec., No. 3, 3–52, 64 figs. [29 refs.] English summary.

ANGEL TORRICO M., R. Primer caso agudo de forma oftalmoganglionar de enfermedad de Chagas comprobado en Bolivia. [**The First Confirmed Case of an Acute Ophthalmo-Ganglionic Form of Chagas's Disease in Bolivia.**] *An. Laboratorio Central*. Cochabamba, Bolivia. 1946, July, v. 1, No. 1, 3–10, 3 figs. [13 refs.]

LEISHMANIASIS.

SHORTT, H. E. **Transmission of Kala-Azar in India : the Case against the Sandfly—a Reply.** *Indian Med. Gaz.* 1946, Aug., v. 81, No. 8, 310–15. [15 refs.]

MALONE, R. H. **Transmission of Kala-Azar.** [Correspondence.] *Ibid.* 333.

In an earlier paper MALONE and BROOKS [this *Bulletin*, 1945, 42, 357] attempted to discredit the view that sandflies transmit kala azar in India and argued that the experimental work which led to the conclusion that *Phlebotomus argentipes* was the actual vector in India was so artificial in its conception that the results obtained were entirely misleading and fallacious. In the correspondence the first of these writers again refers to the joint paper, without adding anything further. In the present paper, the author examines the earlier contributions of these writers point by point and shows clearly that they are not well versed in the literature of the subject and have thus been led to advance specious and superficially plausible arguments in support of their contentions. Those interested in the controversy must consult the papers in the original, which take no account of all the evidence incriminating sandflies in the many areas outside India. *C. M. Wenyon.*

VAN DYKE, H. B. & GELLHORN, A. **Chemotherapy of Experimental Leishmaniasis.** *Proc. Soc. Exper. Biol. & Med.* 1946, Apr., v. 61, No. 4, 403–5.

With the object of discovering more effective remedies for kala azar, 188 new compounds were tested in Syrian hamsters infected with a Sudan strain of *Leishmania donovani*. The drugs were administered intraperitoneally either in solution or in suspensions in 2 per cent. gum acacia. The action was controlled by liver puncture after the hamsters had received six daily injections of the maximum tolerated dose. As controls, untreated hamsters and hamsters treated with the diethylamine ethanol of sodium antimony gluconate (Stibanose) were similarly observed. In no case did any one of the 188 compounds, which included 16 trivalent and 14 quinquevalent antimonials, prove itself to be superior to the control drugs, sodium antimony gluconate, Neostam or Neostibosan. *C. M. Wenyon.*

MESSINI, M. Azione dell'italchina in un caso di leishmaniosi cutanea osservato in Provincia di Roma. [**Action of "Italchina" on a Case of Cutaneous Leishmaniasis seen in Rome.**] *Attualità Med.* Rome. 1940, July–Oct., v. 5, Nos. 7/10, 131–4. [12 refs.]

FEVERS OF THE TYPHUS GROUP.

HEILIG, R. **Typhus in Rajputana.** *Indian Med. Gaz.* 1946, Oct., v. 81, No. 10, 399–400, 2 figs. on 1 pl.

An account of a case of uncertain transmission.

CODELEONCINI, E. Sulle agglutinine della saliva nel tifo esantematico. [**Agglutinins in the Saliva in Exanthematic Typhus.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1946, v. 6, No. 5, 265–72.

The serum and the saliva of 80 typhus patients have been examined for agglutination titres against *Proteus X19* in the Imperial Ethiopian Medical Research Institute. Fifty-seven were Ethiopians, 23 Europeans. Altogether 735 reactions were performed [in two places the number is given as 370]. It was seen that agglutinins did appear in the saliva, but the fact was of little value in diagnosis because the titres varied greatly in the same patient from time to time and were often very low when that of the serum was high; the variation was perhaps due to the varying composition of the saliva. The titres in each of the 80 cases are presented in a table where the contrast is readily seen; as where the serum titre might be 1/5,120 and that of the saliva only 1/80; in another the serum was 1/600, the saliva nil. *H. Harold Scott.*

BERKE, Z. **Inoculation Experiments against Typhus in Afghanistan.** *Brit. Med. J.* 1946, Dec. 21, 944–5.

During 1943 the author carried out a test of the Cox-type typhus vaccine of American origin at Kabul where louse-borne typhus was prevalent. Among 3,122 vaccinated persons there were a few cases of typhus, but none was fatal. Among the unprotected the attack rate was higher and the fatality rate was considerable.

In the course of a series of agglutination tests of sera from persons suspected of having typhus or typhoid fever, 123 patients agglutinated one or more of the commonly used Proteus strains; in 116 cases *Proteus OX19* was agglutinated;

in 73 *Pr. OX2*, and in 33 *Pr. OXK* gave positive responses. The 7 sera that were negative for *Pr. OX19*, but positive for one or both of the other two strains, came from patients whose illness occurred during the month of May or in the autumn.

In May 1937, an outbreak of very severe typhus occurred at Aybak ; all the patients reacted with *Pr. OX2*, but not with *Pr. OX19*, *Pr. OXK*, or six other Proteus strains from the Lister Institute, London.

The number of sera tested is not stated, and the only further information supplied is that plague had been suspected and that " exanthemata were seen in only a few persons, on the medial side of the thigh." *John W. D. Megaw.*

OSBURN, L. W. **Cross-Immunity between South African Epidemic (Louse-borne) Typhus and Murine (Flea-borne) Typhus.** *South African J. Med. Sci.* 1946, Nov., v. 11, Nos. 2/3, 73–7. [14 refs.]

BERKOWITZ, A. P. **A Method for increasing the Infectivity of Yolk-Sac Cultures of the Rickettsiae of Epidemic and Murine Typhus, and South African Tick-Bite Fever.** *South African J. Med. Sci.* 1946, Nov., v. 11, Nos. 2/3, 69–72.

In the course of large-scale preparation of epidemic-typhus yolk-sac vaccines it was found that the yield of rickettsiae was very much greater when the death of the embryo chick was delayed till 10 or 11 days after inoculation than when death occurred about the 6th day.

The delay was brought about by greatly reducing the dose of infecting material as estimated by counting the rickettsiae in smears of yolk-sac suspensions. The technical details of the method are described in the paper.

It is stated that batches of eggs inoculated on the 7th day and harvested 11 days later yield 200 cc. of a strong vaccine for each egg.

The method greatly facilitates the preparation of rickettsial suspensions for agglutination tests ; it is also equally applicable to the cultivation of murine rickettsiae, which can be harvested 12 days after inoculation. In the same way cultures of the rickettsiae of South-African tick-bite fever can be harvested eight or nine days after inoculation instead of the usual four or five days, so that a sufficient yield of rickettsiae for preparing agglutinating suspensions is easily obtained. The author suggests that the method may be equally suitable for yolk-sac cultures of viruses.

Craigie's thionin stain is said to be invaluable for the detection of scattered rickettsiae (see *Canadian J. Res.* Sect. E. 1944, v. 22, 89). [The author appears to have obtained greater and more uniform increases in yield than other workers who have reported the enrichment of yolk-sac cultures by reducing the inoculation dose of rickettsiae, for example BENGTSON [see this *Bulletin*, 1946, v. 43, 19 and 20.] *John W. D. Megaw.*

SMADEL, J. E., JACKSON, E. B., BENNETT, B. L. & RIGHTS, F. L. **A Toxic Substance associated with the Gilliam Strain of** *R. orientalis*. *Proc. Soc. Exper. Biol. & Med.* 1946, June, v. 62, No. 2, 138–40. [12 refs.]

The author found a toxin, which was lethal to mice, in yolk-sac cultures of the Gilliam strain of *Rickettsia orientalis* ; the cultures investigated were those of the 31st and 36th yolk-sac passages. The toxin was neutralized by highly diluted homologous antisera prepared in rabbits and guineapigs. The antitoxic titre of a homologous antiserum was 1–640 whereas the titres of antisera prepared from other strains of the same organism ranged from zero to 1–40.

The antisera tested against the Gilliam toxin were prepared from the following strains of *R. orientalis* :—Karp, two wild-rat strains, Volner, Seerangayee, Host 21, and Kostival. All the above antisera had been found capable of protecting mice from death which normally would have resulted from infection by their homologous strains.

Yolk sacs heavily infected with Imphal, Calcutta, Karp, Kostival, and Host 21 strains of *R. orientalis* were not found toxic to mice. *John W. D. Megaw.*

BELL, E. J., BENNETT, B. L. & WHITMAN, L. **Antigenic Differences between Strains of Scrub Typhus as demonstrated by Cross-Neutralization Tests.** *Proc. Soc. Exper. Biol. & Med.* 1946, June, v. 62, No. 2, 134–7. [10 refs.]

The author presents evidence of important differences between the antigens of three strains of *Rickettsia orientalis*. The strains were :—(1) Kostival (K) isolated from a patient in New Guinea ; (2) Host 21 (H21) isolated from mites caught on a wild bandicoot in the same locality ; and (3) Seerangayee (S) from a patient in South Malaya ; this had been maintained in mice and guineapigs.

Antisera for each of the three strains were prepared by animal inoculation and were tested for their power of neutralizing the three strains of rickettsiae ; the results of the main series of tests are shown in the table.

	Neutralizing Index		
	K strain	S strain	H21 strain
K antiserum (rabbit)	2·7	1·0	0·3
S antiserum (rabbit)	0·9	3·6	1·5
H21 antiserum (guineapig)	2·3	3·7	2·3

K and S antisera effectively neutralized only their homologous strains of infection whereas H21 was active against all the three strains.

The possible explanations of the different behaviour of the strains were regarded as being :—(1) H21 being a "parent" mite strain might be more complete antigenetically than the human strains ; (2) the K and S strains had been passaged more often than H21 through yolk sacs or guineapigs ; (3) H21 antiserum was prepared in guineapigs whereas the other two were prepared in rabbits. *John W. D. Megaw.*

BÉNARD, R. & KERBRAT, G. Un cas de fièvre boutonneuse (maladie de Conor). [**A Case of** *Fièvre boutonneuse* **(Conor's Disease).**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1947, Nos. 1/2, 29–32.

WICHT, J. F. & RABKIN, Rachel. **A Note on Tick-Bite Fever.** *South African Med. J.* 1947, Jan. 11, v. 21, No. 1, 30–31.

Report of a case.

FENNER, F. **The Epidemiology of North Queensland Tick Typhus: Natural Mammalian Hosts.** *Med. J. Australia.* 1946, Nov. 9, v. 2, No. 19, 666–8.

Complement-fixation tests were carried out on sera of 111 mammals collected in three localities from one of which five cases of North Queensland tick typhus had been reported (see this *Bulletin*, 1947, v. 44, 202].

The antigen was prepared from yolk-sac cultures of one of the strains of rickettsiae isolated by FUNDER and JACKSON [this *Bulletin*, 1947, v. 44, 204].

Details are given of the number of animals captured in each locality, and of the ectoparasites found on the animals of each species.

Sera of eight animals reacted at titres of 1–4 or over, and five of these were collected in the rain-forest area where cases of the disease had occurred. The reacting animals were:—two among 42 Johnstone's opossums (*Trichosurus vulpecula johnstonii*); two among 11 rufous rat-kangaroos (*Aepyprymnus rufescens*); two among 32 short-nosed bandicoots (*Isoodon obesulus*); one among 10 Atherton uromys (*Uromys sherrini*); and one among 5 long-nosed bandicoots (*Perameles nasuta*).

On five of the reacting animals *Ixodes holocyclus* ticks were found; on two others *Haemophysalis humerosa* were found; on the remaining reactor no ticks were found.

Various species of fleas and mites were detected on many of the animals; among the eight reactors, four were infested by fleas of three species, and six harboured mites of four species.

Suspensions of pools of ticks from seven of the reacting animals and from 28 others were inoculated intraperitoneally into guineapigs, but the results were negative.

The presumed vector, *Ixodes holocyclus*, and most of the animals assumed to have been infected, are stated to have a wide range of distribution in eastern Australia. *John W. D. Megaw.*

ROTENBURG, S. S. [**Prolonged Attacks of Fever of Obscure Origin.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 37–44, 2 figs. [In Russian.]

The author describes cases of a disease of obscure nature encountered in Central Asia and characterized by intermittent paroxysms of fever of short duration with apyrexial intervals of different length, the temperature rising to 39–40·5°C. The course of the disease was benign, its duration sometimes exceeding one year. The paroxysms were accompanied by neutrophil leucocytosis, and in a few cases by enlargement of the spleen and liver. Neither malaria parasites nor spirochaetes were detected in the blood of the patients. Burnet's and Wright's reactions were negative. Inoculation of guineapigs and mice with the blood of the patients produced no infection. Treatment with sulphidine, streptocide, urotropine, and with antimalarial drugs had no effect.

While malaria, tick-borne relapsing fever and brucellosis could be entirely excluded, there remains the remote possibility of the disease representing Volhynian fever with an atypical course and manifestations. *C. A. Hoare.*

PETRJAEV, E. D. [**Tick Fever in the Transbaikal Region.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 84–5. [In Russian.]

The author records the occurrence in the Transbaikalian region of tick-borne fever of a type previously reported from other parts of Soviet Asia. The vector proved to be the tick *Dermacentor nuttalli*, wild specimens of which were found to be naturally infected, as shown by experimental infection of guineapigs. The disease is first manifested 4–5 days after the patient has been bitten by a tick. At the site of the bite there appears a small necrotic spot surrounded by infiltrated tissue. The patient complains of weakness, chill and headache. By the third day the temperature rises to 40°C., after which it gradually drops until by the 8th–10th day it is normal. On the 4th–6th day the whole body, including the palms of the hands and face, becomes covered with a roseolar-papular rash which persists for 6–8 days. After its disappearance, there remain

faintly pigmented spots on the skin. The spleen and liver are not enlarged. During the first days of the disease there is leucocytosis (9,000–12,000 per cu. mm.) and moderate lymphopenia.

The Weil-Felix reaction remains negative during the entire febrile period (first 8–10 days of the disease), but by the 11th-14th day of the disease, when the temperature is normal, the reaction with *Proteus OX19* is positive in titres of 1 : 200–1 : 400. On the 10th and 16th days of convalescence, the titre of agglutinins reaches 1 : 3,200–1 : 6,400, and on the 42nd day it is 1 : 800. The present finding shows that all Siberia, Cisbaikalia, Transbaikalia, the Mongolian Republic and the Soviet Far East represent a single endemic area of a new and incompletely studied disease, which it is proposed to name " The Eastern Typhus Fever ". *C. A. Hoare.*

YELLOW FEVER.

HADDOW, A. J., GILLETT, J. D. & HIGHTON, R. B. **The Mosquitoes of Bwamba County, Uganda. V. The Vertical Distribution and Biting-Cycle of Mosquitoes in Rain Forest, with further Observations on Microclimate.** *Bull. Entom. Res.* 1947, Jan., v. 37, Pt. 3, 301–30, 2 pls. & 11 figs. [14 refs.]

Haddow and those who work with him continue to publish studies on the mosquitoes of an area of rain-forest in Uganda, close to the Congo border. The yellow fever virus has been isolated in this area from a human case and from *Aëdes simpsoni.*

Within recent years, the virus has been isolated more than once from mosquitoes under circumstances which suggest that it has been derived from some animal other than human beings, and immunity to yellow fever has been demonstrated in a high proportion of monkeys of several species, but not in other wild mammals. It is found that some of the monkeys which live in the tree-tops and rarely come to the ground, including a species of Colobus, have this immunity, though they seem to have no contact with man or with *Aëd. simpsoni.*

As there seems to be an indication that transmission might be occurring in the tree-tops, the author made collections of mosquitoes from platforms at various levels between the ground and 80 ft. This was carried out in an isolated patch of primary rain-forest : it had an area of about one square mile and carried a population of some 400 monkeys belonging to nine species. On the platforms, mosquitoes were caught by relays of small boys throughout the twenty-four hours on a number of different occasions, the human being acting as bait for the mosquitoes. Forty species of mosquitoes, including several new to science, were captured. They were sorted by species and other groups and 46,000 of them sent to the laboratory at Entebbe where they were inoculated into rhesus monkeys to see whether the virus was in the mosquitoes. The virus was recovered once only, from a batch of *Aëdes* of twelve species mixed : among these species was *Aëd. africanus*, which is a known vector in the laboratory and is under suspicion.

In the present paper, the authors analyse an enormous amount of fact about the level in the forest at which different mosquitoes occur, the time of day or night at which they bite and the abundance in the rains and dry season.

The reader notes that *Anopheles funestus* is not common, though it has been caught at all levels from the ground upwards. It is thought that it breeds in

the swamps outside the forest. *Anopheles gambiae* occurred in numbers which astonished the authors, who were familiar with it in its more ordinary haunts. Some 30,000 individuals were caught during forty day and night catches, and constituted 93 per cent. of all the mosquitoes. This insect was commonest at ground level, but occurred on all the platforms, both in the dry and the wet season. Almost half the bites took place between 2 and 6 a.m. with a peak just before dawn. The author relates this to the fact that temperature falls regularly through the night, though relative humidity remains nearly constant during that period. A small number of individuals were found biting at any time of the day in forest. The abundance of this insect in a place which is generally without human inhabitants is so remarkable that a critical examination has been made of adults and larvae: they are not found to differ in any respect from normal *gambiae*.

The species of *Aëdes* showed a great diversity of habit. Some are ground-haunting, others (among them the sub-genus *Stegomyia*) live higher up or in the tree-tops, and these show a very great reduction in the dry season, presumably because they breed in little places, such as rot holes, which tend to dry up in the absence of frequent rain. Of the arboreal Culicines, *Aëd. africanus* was found to be the most numerous. It was most abundant at 50 to 60 ft. from the ground and bit in the period from 6 to 10 p.m., with an extremely well-marked peak one hour after sunset.

Rather similar notes are given about several species of *Taeniorhynchus* and *Eretmopodites*.

The authors have given much time to recording temperature and relative humidity at all levels in the forest. Throughout the twenty-four hours these elements of climate show little difference between ground level and 16 feet. At 30 ft., and still more at higher levels, temperature is higher than at the ground, especially at mid-day: there is a corresponding lowering of relative humidity. A small series of readings of light, recorded on an arbitrary scale, were also made. It is not at present possible to find any convincing relation between these observations on climate and the distribution or activities of the mosquitoes. The subject appears to be one for testing in the laboratory, where it would be possible to change any of these conditions at will and independently of the others. *P. A. Buxton.*

HOFFMAN, W. H. El tratamiento precoz de la fiebre amarilla. [**Early Treatment of Yellow Fever.**] *Africa Méd.* Lisbon. 1946, May–June, v. 12, Nos. 5/6, 99–107.

By "early" the author implies both "timely" in the disease itself and "prophylactic" in endemic areas of yellow fever. Having heard of the work of BAY, BANFI and TANURI (*Semana Médica*, 1942, 593) in the Argentine on the protection of dogs from the effects of chloroform on the liver by administration of vitamin K, or its synthetic analogue *Synkavite Roche*, and noting that in yellow fever the liver destruction is so marked a feature, he suggests the use of this vitamin or its analogue for early treatment of patients, that is, in the first two or three days of the disease to obviate the fatal issue, and also prophylactically in non-immunes in endemic foci. No details are given or suggestions regarding dosage. The rest of the paper is an interesting sketch of the history of yellow fever in Cuba, and particularly in Havana. Professor Hoffmann has been intimately connected with yellow fever research and progress in Cuba since the days of Finlay and Guiteras. *H. Harold Scott.*

DENGUE AND ALLIED FEVERS.

MACKERRAS, I. M. **Transmission of Dengue Fever by** *Aëdes* (*Stegomyia*) *scutellaris* **Walk. in New Guinea.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 295–312, 5 figs. [13 refs.]

The author shows that dengue may be transmitted by a forest-living mosquito, in remote areas in New Guinea.

Classical dengue is familiar to Australian writers ; it occurs in settled areas in tropical Australia and in ports in islands further north, such as Port Moresby, New Guinea. During the war period a very similar disease appeared among troops in jungle areas in several parts of New Guinea. *Aëdes aegypti* could not be found, nor *Aëd. albopictus,* Sk (a proved vector in Formosa, Sumatra and the Philippines). When an outbreak occurred in jungle areas on the south side of New Guinea, *Aëdes funereus* was investigated, with negative results. A second epidemic on the north coast, near Lae, provided an opportunity to test *Aëd. scutellaris,* and other Culicines. The mosquitoes were caught as adults (or bred in a small number of cases), and sorted into cages by species. Those in each cage were then fed more than once, on different men suffering from the disease, and then flown to Sydney to be tested on volunteers. *A. scutellaris* transmitted the infection to three men and it was passed on to other volunteers, all of whom showed typical symptoms. The original three were then shown to be immune to inoculation of infected blood. The clinical observations, with temperature charts, are given in some detail, and maintain the author's view that the disease was correctly diagnosed as dengue.

Other mosquitoes (*Armigeres* spp., etc.) were tested in a similar way. The material was less abundant and the number of bites given in Australia not very high. Transmission did not result.

The authors point out that the incrimination of *Aëd. scutellaris* serves to explain the severe outbreak on the north coast of New Guinea, where that insect was abundant. They admit that their findings, while settling one question, raise another : why is dengue unknown in wide areas in Melanesia and Polynesia ? Is it (as a few unpublished facts suggest), that some of the local varieties of this widely spread mosquito are not good transmitters, though they bite man so freely ? The cases of dengue in rural areas not far from Port Moresby also remain unexplained, for the authors failed to find *Aëd. scutellaris* there.

As the mosquitoes were given more than one infecting meal, the period of development of the virus in the insect is not known. It is likely to be 13 to 19 days, longer than has been recorded in other mosquitoes [temperature not stated].

Aëd. scutellaris breeds in rain water in empty coconut shells, tree holes and forks, large fallen leaves, and old utensils, choosing water which is not heavily contaminated. The adults do not fly far. They enter tents to feed, but do not rest in them. The biting period is generally restricted to a period just after dawn and at sundown. The insect may be controlled by searching out breeding places ; cutting grass and scrub round a camp assists this. Fine drifting mist of DDT may be found capable of killing the mosquito or its larva throughout an area. *P. A. Buxton.*

KOPROWSKI, Hilary & COX, H. R. **Adaptation of Colorado Tick Fever Virus to Mouse and Developing Chick Embryo.** *Proc. Soc. Exper. Biol. & Med.* 1946, June, v. 62, No. 2, 320–22.

The author succeeded in infecting dba (dilute brown agouti) mice by the intracerebral route with serum from a hamster infected with the virus of

Colorado tick fever. The serum was obtained from Dr. Florio who had already maintained the virus in hamsters through 30 passages [see this *Bulletin*, 1945, v. 42, 118].

Successive passages were made from brain to brain in dba and Swiss mice and there was a considerable increase in virulence so that by the sixth passage all the inoculated animals died. The chief concentration of the virus was in the brain and spinal cord, but the heart, spleen, lungs and blood, also contained the virus.

Identification of the virus was effected by neutralization tests carried out on human, hamster, and mouse antisera, of which very small doses mixed with heavily infected brain substance protected mice from fatal infection by the intracerebral route.

A unit dose of immune human serum from a patient who had been attacked three years previously was found capable of neutralizing 1,349 LD_{50} doses of the virus, and a corresponding dose of hamster immune serum neutralized 525 LD_{50} doses of the virus.

Up to the time of writing 23 consecutive brain-to-brain passages have been made. With material from the brain of a mouse of the 12th passage yolk sacs were inoculated and 12 yolk-sac passages have been carried out.

John W. D. Megaw.

GOSWELL, G. **A Further Report of an Epidemic of Acute Polyarthritis.** *Med. J. Australia.* 1946, Dec. 21, v. 2, No. 25, 861–3.

PLAGUE.

MACCHIAVELLO, A. **A Focus of Sylvatic Plague on the Peruvian-Ecuadorian Frontier.** *Science.* 1946, Dec. 6, 522.

In South America, hitherto, true sylvatic plague appears to have been reported only from Argentina [DE LA BARRERA, this *Bulletin*, 1940, v. 37, 423]. It has also been believed up to now that plague on the Peru-Ecuador frontier is strictly rural, but in May 1946, extensive epizootics began at both sides of the frontier.

The author's investigations were made in the Encuentros zone of Peru, south from the Ecuadorian border. The country is mountainous with small permanent rivers.

The principal focus of sylvatic plague was in the mountains, La Mesa and Cortezo, where vegetation is dense and the climate is continental. Corn is cultivated on the mountains in small scattered fields, cleared for the purpose.

The author designates this outbreak as sylvatic plague on the following grounds :—

1. The absence of domestic rats and their fleas, which alone transmit plague in the rest of the country.

2. The sparse population, with scattered dwellings and absence of significant domestic factors : yet 19 human cases of bubonic plague occurred there, but nearly all the patients were shown to have been infected in the mountain cornfields during the harvest.

3. An intense epizootic among squirrels and native field rats inhabiting the rocks and wooded areas on the slopes and mountain heights.

4. The presence of plague infection in 8 squirrels and 5 dead rats in the wooded areas bordering the cornfields.

5. Infestation of these animals by many mites, ticks, lice and fleas, all the last-named being *Rhopalopsyllus*, of possibly more than one species. These fleas live away from their animal hosts in the cornfields, and many were collected on the investigators' clothing in these fields.

6. The finding of 2 species each of mice and squirrels and four of rats, all of which (with their ectoparasites) are being classified. None of the species so far identified has been involved in plague elsewhere in Peru.

Studies of all these factors are being continued experimentally, but the author claims that the evidence already available supports the claim that this outbreak should be designated as sylvatic plague. *H. J. O'D. Burke-Gaffney.*

GIRARD, G. L'association pneumocoque-bacille de Yersin "in vivo et in vitro". [**The Association of the Pneumococcus and the Plague Bacillus.**] *Ann. Inst. Pasteur.* 1946, Sept.–Oct., v. 72, Nos. 9/10, 708–18.

The conjunction of the pneumococcus with the plague bacillus in various forms of plague has long been known and has on occasion produced mistaken diagnosis. The significance of the association, which affects especially the pathogenic and bile-soluble pneumococci, is obviously important for the diagnosis of plague pneumonia. It is here that the inhibitory, or antibiotic, action of pneumococcus on the plague bacillus in the sputum of the suspected case may lead to error. That error is perpetuated by providing cultural conditions favourable to the growth of the pneumococcus or by using test animals for inoculation which are particularly susceptible to pneumococcus infection. Conditions must be arranged to favour growth and manifestation of *P. pestis*, and these are: (1) to incubate cultures at 20°C. to 26°C. and not at 26°C. to 34°C., (2) to use the guineapig for inoculation of, or scarification with, the test material instead of the pneumococcus sensitive mouse.

There is some evidence to show that the pneumococcus may exert an antibiotic action on the plague bacillus so as to abort or, at least, delay its onset. This action is not specifically directed, but applies to quite a number of other organisms. It has a very special application in plague pneumonia or in the diagnosis of a plague septicaemia. In plague the incubation period has been laid down internationally as six days, but that relates practically to bubonic plague. The incubation, however, may be prolonged, probably by pneumococcus action, in the case of primary plague pneumonia. In Madagascar the authorities have accordingly fixed a limit of 10 days quarantine detention for contacts as their statutory minimum. Plague pneumonia is brought about by the plague bacillus purely and cannot be regarded as either initiated or promoted by the pneumococcus. *W. F. Harvey.*

SHAMANNA, D. & HEDGE, K. V. **Some Clinical Impressions of a Plague Epidemic.** *Indian Med. Gaz.* 1946, Oct., v. 86, No. 10, 432–3.

An account of 26 patients in Saklaspur (Mysore) treated with sulphadiazine: 20 recovered.

GRASSET, E. **Control of Plague by means of Live Avirulent Plague Vaccine in Southern Africa (1941–44).** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 275–94. [11 refs.]

Examples of the use of live avirulent plague vaccine as a means of controlling human outbreaks are becoming numerous. In South Africa, sylvatic plague is a problem; the enzootic area is huge, extending from the Cape Karoo and the High Veld north-westward through the Kalahari desert to Bechuanaland, South-West Africa and Angola.

Vigorous measures have been taken to apply vaccine-prophylaxis and to collect data during human plague outbreaks. The vaccine, of K/120 South Africa and E V Madagascar strains, was a live suspension in concentration of 1,000 million organisms per cc., given subcutaneously, in a dose of 1 cc. by single injection. Experiments in dehydration of the vaccine at low temperatures by means of the lyophile process showed storage capabilities up to 2 years with "only little attenuation in the antigenic properties."

As a method of mass immunization carried out to a total of 40,000 individual doses, the vaccine proved eminently satisfactory inasmuch as the reactions were mild. Fourteen outbreaks of plague have been investigated and out of one total of 24,000 persons immunized there occurred only seven pneumonic, seven bubonic and one septicaemic case of plague. The last case recovered. Protection from the immunization is claimed to be effective by the 5th day and to be maximum by the 10th day after inoculation. *W. F. Harvey.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

SHUTE, D. **Liver Damage in Amoebiasis.** *Brit. Med. J.* 1947, Feb. 1, 172–5. [30 refs.]

Despite the close connexion between amoebic dysentery and hepatic disease there have been few attempts at investigating the liver condition other than by clinical methods.

There have been investigations into the hippuric acid synthesis, the Takata-Ara and the Weltmann coagulation reactions; the present investigation is concerned with Hanger's cephalin-cholesterol flocculation test (C.C.F.T.) which seemed the most promising to apply to this problem and which is stated to be the most sensitive means of demonstrating disease of the liver parenchyma.

The patients selected were all Europeans; Asiatics were excluded on account of the high incidence of malaria and helminthic infestations.

The diagnosis of amoebiasis was established in every case by demonstration of the trophozoites or cysts of *Entamoeba histolytica* in the faeces or in material obtained by sigmoidoscopy or by proctoscopy.

The C.C.F.T. was done on each patient's serum directly the diagnosis was made, approximately half-way through the course of anti-amoebic treatment and on its completion.

After 14 days' sick leave, the patients returned to hospital for test of cure and during this period the final C.C.F.T. was performed.

The scheme of treatment was the routine course advised by ADAMS at the Liverpool School of Tropical Medicine. Hanger's test was done (1) before the first dose of emetine hydrochloride, (2) between the 9th and 11th days of the sterilizing course, (3) within two days of completion of the course, and (4) on return from sick leave. On clinical grounds, the cases were divided into four groups:—(1) Acute amoebic dysentery, (2) chronic amoebic colitis, (3) amoebiasis presenting with unusual symptoms, (4) amoebic hepatitis. Cephalin was extracted from sheep brain and made up with cholesterol in ether. The technique of Hanger was followed, except that the final readings for the degree of flocculation were made after a 24 hours' interval, as DICK (1945) has stated that a considerable proportion of normal sera will cause some flocculation after 48 hours.

Normal controls were included as a routine with every batch of sera from amoebiasis cases.

It seemed possible that any liver disease demonstrable in cases of intestinal amoebiasis may be due to secondary bacterial invaders and their toxins. In a series of 73 cases of amoebiasis (excluding those proved to have hepatic involvement) 37 (50·6 per cent.) gave evidence of damage to the liver parenchyma —that is ++, +++, or ++++ flocculation in Hanger's C.C.F.T.

These 37 cases were fairly evenly distributed amongst the three clinical groups, whilst there was no great difference in the incidence of liver involvement between the groups. The symptomatology and physical signs did not appear to afford any indication of the cases in which it was possible to anticipate hepatic damage.

Institution of suitable anti-amoebic therapy produced a rapid recovery of the liver, as indicated by the C.C.F.T.

A very small series of hepatic amoebiasis investigated did not justify attempts to draw any conclusions.

The actual pathological changes present in the liver are probably generalized increase of portal connective tissue, lymphocytic infiltration and degenerative changes. *P. Manson-Bahr.*

CHAUDHURI, R. N. & CHAKRAVARTY, H. **A Case of Carcinoma of the Colon with Amoebic Infection.** *Indian Med. Gaz.* 1946, Oct., v. 86, No. 10, 422–3, 3 figs. on 1 pl.

BLANC, F. & SIGUIER, F. Les facteurs de gravité, de rechute, de chronicité et d'échecs thérapeutiques de l'amibiase en milieu tropical. [**The Factors of Gravity, Relapse, Chronicity and Therapeutic Failures in Amoebiasis in the Tropics.**] *Bull. et Mém Soc. Méd. Hôpit. de Paris.* 1946, Nos. 26, 27 & 28, 476–7.

RAIL, G. A. **A Comparative Study of the Therapeutic Effects of some of the Drugs used in the Treatment of Amoebic Dysentery.** *J. Trop. Med. & Hyg.* 1947, Jan., v. 50, No. 1, 3–12.

The treatments used for purposes of comparison were six in number and fifty cases were included in each series.

Series I. Emetine hydrochloride gr. i injections for eight days, four days rest, and then gr. i daily for a further four days. Total dosage, 12 gr. Carbarsone 0·25 gm. daily for ten days, commencing on the first day of rest and continuing for two days after cessation of emetine. This—as the standard Eastern Army treatment for amoebic dysentery in January 1944—was taken as a good basic treatment for comparison.

Series II. Kurchi bismuth iodide, 10 gr., for ten days. Carbarsone 0·25 gm. for ten days. The two given concurrently.

Series III. Enterovioform 0·5 gm. for twelve days. Carbarsone 0·25 gm. for ten days. The latter given concurrently with the last ten days of enterovioform.

Series IV. Emetine and carbarsone as in treatment I. Sulphapyridine 2 gm. *statim* and then 1 gm. four-hourly for a total of 13 gm. given on the first two days of emetine.

This latter addition was decided upon when it was judged that some secondary bacterial invasion of the rectal mucosa had taken place.

Series V. Combined treatment of emetine bismuth iodide—total dosage 19 gr. with retention enemata of 2½ per cent. chiniofon for ten days.

Series VI. Emetine hydrochloride, 1 gr. daily for twelve days. Chiniofon 2½ per cent. retention enemata as in Series V for the last ten days of emetine injections.

Cases in each series were divided into :—

(1) Fresh injections.

(2) Relapsed cases—all who had had an attack of amoebic dysentery within the last six months.

The diagnosis was based on the finding of vegetative forms of *Entamoeba histolytica* in the faeces or by sigmoidoscopic swab. *Cysts* alone were not taken as proof of amoebic infection.

The criteria on which conclusions were based were arranged under three headings:—(*a*) symptoms, (*b*) sigmoidoscopic findings, and (*c*) stool examinations. All patients were sigmoidoscoped both before and after treatment ; the second examination took place on the seventh day following the cessation of treatment. Faeces were examined on six days following treatment, and again on the 19th, 20th and 21st days. It is acknowledged that the 21-day period is very short.

Results.

Series I (Emetine and carbarsone—18 days). No encysted forms of *E. histolytica* were observed in any of the 50 cases following treatment : probably this was due to carbarsone. It is concluded that this treatment is effective in removing symptoms and healing intestinal lesions, but recurrences took place in 18 per cent. within 21 days.

Series II (Kurchi bismuth iodide and carbarsone—10 days). All symptoms, some severe, subsided within four days which raised hopes as to the therapeutic value of this combination, but the effect was short-lived. Within six days, in four cases, diarrhoea with blood and mucus containing vegetative *E. histolytica*, supervened. Although from the sigmoidoscopic aspect the treatment appeared to have been extremely beneficial, the amoebicidal action was low and the total relapse rate was 48 per cent.

Series III (Enterovioform and carbarsone—12 days). In 13 out of 33 cases, inflammatory lesions in the rectal mucosa were still present at the end of the course. It was concluded that this method is of some value in the acute stage, but of little use in the chronic.

Series IV (Emetine and Carbarsone with sulphapyridine—18 days).

Sigmoidoscopy revealed a diminution of the " inflammation cases ", but in two the ulceration persisted throughout treatment. As compared with Series I there was a marked reduction in the numbers with mucosal inflammation and this was ascribed to sulphapyridine.

Series V (Combined treatment—10 days). In one case only were encysted forms found on completion of treatment : sigmoidoscopic appearances were normal and stools negative at the end of 21 days. Healing of the ulcers was less rapid than that observed after emetine and carbarsone.

It is concluded that, apart from the healing of ulcers, this combination is superior to that of emetine and carbarsone in the production of a 21-day cure.

Series VI (Emetine—12 days and Chiniofon during the last 10 days). It was concluded that this treatment is as effective as that of emetine and carbarsone in the alleviation of symptoms and in the production of intestinal healing.

It appeared to the author that those drugs containing emetine, whether in the form of E.B.I. or the hydrochloride, are superior in amoebicidal action to those which do not. This fact, in combination with the undoubted value of chiniofon by retention enemata, has induced him to devise a treatment which combines concentration with safety :—

(1) Emetine gr. 1 daily for ten days.

(2) E.B.I. and chiniofon from 6th to 15th days, as in Series V.

(3) Sulphapyridine 2 gm. *statim*, and then 1 gm. four-hourly to a total of 13 gm. commencing on the first day of emetine. Over this period the patient's diet should be of medium caloric value and low residue. From the sixth to

fifteenth days, strict confinement to bed is insisted upon. The total dosage of *emetine* (including the E.B.I.) is 14¾ gr.

[The shortcomings of these results are patent, as it is not possible to appraise the final effects of any particular line of therapy in amoebiasis after so short an interval as three weeks, though the authors' difficulties under the conditions of military service are fully appreciated.] *P. Manson-Bahr.*

BLANC, F. & SIGUIER, F. Le traitement des amibiases chroniques et à rechutes par l'association pénicilline-émétine-sulfamides. Premiers essais thérapeutiques. [**Treatment of Chronic and Relapsing Amoebiasis with a combination of Penicillin, Emetine and Sulphonamides.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 26, 27 & 28, 471–5.

A brief record of the treatment of ten cases of chronic relapsing amoebiasis and secondary colitis with emetin and penicillin, and in some with sulphaguanidine in addition. The immediate clinical response in all but one case was dramatic. *A. R. D. Adams.*

KNOLL, Elta W. & HOWELL, Katharine M. **In Vitro Effect of Penicillin on** *Endamoeba histolytica. Arch. Pathology.* 1946, Dec., v. 42, No. 6, 594–7.

Little or no effect was found on either trophozoites or cysts.

KESSEL, J. F. & MOORE, F. J., with the technical assistance of F. M. KAPLAN & R. SCHIRESON. **Emergency Sterilization of Drinking Water with Heteropolar Cationic Antiseptics. I. Effectiveness against Cysts of** *Endamoeba histolytica. Amer. J. Trop. Med.* 1946, May, v. 26 No. 3, 345–50. [16 refs.]

The authors have tested a number of heteropolar cationic antiseptics, or, as they are sometimes termed, synthetic cationic detergents for their powers of destroying cysts of *Entamoeba histolytica* in drinking water. The tests were carried out by suspending cysts (10,000 per cc.) in varying dilutions of the antiseptics for 10 minutes at a temperature of 20°C. The cysts were then washed and inoculated to a culture medium. If amoeba did not develop during the course of five days the cysts were regarded as killed. At the same time oral toxicity tests were carried out on mice. Three of the substances tested were effective in dilutions of over 1/80,000, the safest being n-hexadecyl dimethyl 2-hydroxyethyl ammonium chloride. A few of the more effective were sampled for taste and were found to be slightly medicinal and astringent. Further studies are being undertaken with the object of discovering methods for the removal of excess of the substances from water after sterilization has been completed. It has also to be determined whether signs of toxicity would be noted when they were consumed over long periods. *C. M. Wenyon.*

WATSON, J. M. **Studies on the Morphology and Bionomics of a Little-Known Holotrichous Ciliate—***Balantiophorus minutus* **Schew. Part III. Coprophilic Habits and the Effect of Urine.** *Parasitology.* 1946, Aug., v. 37, Nos. 3/4, 138–51. [38 refs.]

In this paper the author gives an account of his studies on *Balantiophorus minutus* from the point of view of its ability to develop in normal and abnormal human faecal material. The interest of the observations lies in the fact that this ciliate, which is an occasional inhabitant of tap water and has been not infrequently seen in diarrhoeic stools, was regarded by SCHAUDINN as a new species of *Balantidium* (*B. minutum*) and by many others who followed him. The author's investigations show that the ciliate grows readily in normal faeces, whether diluted or not. It was remarkable that it failed to grow in

undiluted faeces of soft or liquid consistency from various cases of intestinal disorder. Frequently dilution of such faeces failed to give a suitable medium for growth. The chief reason for the failure was the high osmotic pressure in the liquid stools and the presence of bile salts, which are highly toxic to the ciliate. Two other factors which hinder growth are the presence of drugs and contamination with urine. Experiments in mice showed that the cysts of the ciliate were incapable of passing uninjured through the alimentary canal. In no case was it possible to obtain cultures from the mice. *C. M. Wenyon.*

D'IGNAZIO, C. Sulle parassitosi intestinali di Etiopia. [**The Intestinal Parasites of Ethiopia.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1946, v. 6, No. 5, 227–36.

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

DE MEILLON, B. & GOLBERG, L. **Development of *Ornithodorus moubata* on Normal and Thiamin-deficient Rats.** [Correspondence.] *Nature.* 1947, Feb. 1, 171.

Little work has so far been published on the effect of feeding blood-sucking arthropods on mammals whose own diet has been abnormally deficient in vitamins and other factors. The authors of this communication previously showed that bed bugs (*Cimex lectularius*) and nymphal ticks were adversely affected when fed on rats reared on a diet deficient in thiamin [see *Bulletin of Hygiene*, 1946, v. 21, 838]. They have now shown that whereas *Ornithodorus moubata* has four moults before reaching maturity when fed on normal rats, it has five when fed on thiamin-deficient individuals. The period between moults is also prolonged in the latter case, so that the development takes some 80 days, instead of the 41 days taken when normal rats are used. The larger nymphs show some reluctance to feed on the deficient rats. *Kenneth Mellanby.*

CALERO, C. **Relapsing Fever on the Isthmus of Panama. Report of 106 Cases.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 761–9. [21 refs.]

The author discusses the clinical aspect of relapsing fever on the Isthmus of Panama, based on the records of 34 patients at the Santo Tomas Hospital, Panama City, from 1927–1944, and of 72 patients from Gorgas Hospital, on the Canal Zone, from 1907 to 1944 inclusive.

The aetiological agent, *Spirochaeta neotropicalis*, a variety of *S. recurrentis*, is usually transmitted by *Ornithodorus venezuelensis* but also by *O. talaje*, from animals to man. The incidence of the disease is very low, not more than 0·11 per 1,000 hospitalizations. It generally occurs among field workers between 14 and 36 years of age and seems to exist throughout all areas of the republic.

The clinical symptoms are almost identical to the cases of relapsing fever described in Texas [see this *Bulletin*, 1936, v. 33, 347]. The prognosis is good, no deaths having been reported. Treatment with an initial dose of 0·3 gm. of neosalvarsan or neoarsphenamine, injected intravenously, followed 24–48 hours later by 0·45 gm. of the same drug, gives satisfactory results. *E. Hindle.*

LEBON, J., CHOUSSAT, H. & DUBOUCHER, G. Sur quelques formes nerveuses de la fièvre récurrente cosmopolite. [**Some Nervous Forms of Cosmopolitan Relapsing Fever.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 26, 27 & 28, 448–50.

D'IGNAZIO, C. & CODELEONCINI, E. Atipie della febbre ricorrente dello Scioa. [**Atypical Relapsing Fever in Scioa.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1946, v. 6, No. 5, 237–42.

The authors mention in general terms—no cases are detailed—certain unusual forms of relapsing fever which have come under their observation in Addis Ababa. Six such atypical forms are spoken of: (1) With severe *hepatic* symptoms, enlarged liver, subicterus, with much biliary vomiting, diffuse tremors and haemorrhages (see below) and rarely coma and hyperpyrexia. (2) *Haemorrhagic* form, with epistaxis, haematemesis, intestinal, renal, cerebral and cutaneous (petechial) haemorrhages, often associated with the hepatic form. Both these are more common in the natives than in Europeans. (3) *Pseudo-dysenteric*, with repeated and uncontrollable vomiting and mucous and muco-sanguinolent stools, colic and perhaps tenesmus. (4) *Pulmonary*, with a picture typically like that of lobar pneumonia. They have seen 18 such cases between 1937 and 1945. (5) *Meningo-encephalitic.* (6) *Pseudo-rheumatic*, with pain in muscles, joints and bones, but failing to respond to the usual anti-rheumatic remedies.

As regards treatment, the rheumatic form responds to bismuth and arsenic; in the pulmonary form much is hoped for from penicillin; in the haemorrhagic form vitamin K has proved beneficial. In the early stages of the disease, they have tried various remedies, insulin, cardiac tonics, liver and adrenal preparations and glucose injections with varying effect—their very multiplicity indicating that there is no certain remedy. *H. Harold Scott.*

WYLIE, J. A. H. **The Relative Importance of the Renal and Hepatic Lesions in Experimental Leptospirosis Icterohaemorrhagica.** *J. Path. & Bact.* 1946, July, v. 58, No. 3, 351–8, 6 figs. on 2 pls. [28 refs.]

Routine autopsies of guineapigs dying from a strain of *Leptospira icterohaemorrhagiae* (isolated from the kidneys of rats infesting a P.O.W. camp in which there had been two established cases of Weil's disease) revealed a considerable variation in the extent and degree of the liver necrosis observed. The administration of excess methionine in the diet was followed by a significant reduction in the incidence of liver necrosis but did not affect either the survival time or the progress of renal failure. All animals dying from the leptospirosis developed severe kidney lesions which showed histologically severe engorgement of the glomeruli and tubular damage similar to that described in incompatible blood transfusion, traumatic anuria and blackwater fever. The author considers that the death of the guineapigs inoculated with his strain of Leptospira resulted from renal failure. The latter is probably an example of the "syndrome of renal anoxia" [MAEGRAITH *et al.*, this *Bulletin*, 1945, v. 42, 968]. *B. G. Maegraith.*

WILLIAMS, M. H. C. **Treatment of Renal Failure in Weil's Disease by Spinal Anaesthesia.** *Lancet.* 1947, Jan. 18, 100–101, 2 figs.

The author reviews the evidence suggesting that renal failure in Weil's disease and certain other conditions may result from "renal anoxia" arising from ischaemia of the renal cortex [MAEGRAITH, HAVARD & PARSONS, this *Bulletin*, 1945, v. 42, 968]. If the reduction in glomerular flow were the result of vascular spasm, "paralysis of the sympathetic nerves" should be useful in the treatment of such conditions. Splanchnic block has been tried with success in the treatment of anuria following blood transfusion and abortion. ROBERTSON [this *Bulletin*, 1947, v. 44, 428] treated three cases of anuria in Weil's disease with high spinal anaesthesia and reported recovery in one case.

Dr. Williams suggests that sympathetic paralysis should be started in Weil's disease in the oliguric stage, before anuria has developed. He describes a case in which such a procedure was successful.

The patient, aged 61, was admitted to hospital suffering from Weil's disease. He was given a pint of plasma intravenously and an intramuscular injection of methedrine 30 mgm. The plasma was followed by 4·3 per cent. sodium sulphate by slow drip and 0·5 mgm. "Digoxin" orally. On the day following admission, catheterization produced 8 oz. of urine which was acid, contained albumin, bile, leucocytes, some red cells and occasional casts. Unfortunately, the exact amounts of urine passed subsequent to this and prior to anaesthetic treatment were not recorded, but the patient was "still secreting small quantities." The case note continues: "At 6 p.m. there had been no increase of urinary output so high spinal anaesthesia (16 cc. of light 'Nupercaine', the patient sitting up for 55 sec.) was administered producing skin anaesthesia up to the level of D7. By the next morning he had received 105 oz. of fluid and had passed 52 oz. urine." The diuresis continued and after a day's lag the blood urea N (321 mgm. per cent. on admission) fell rapidly, reaching normal limits in about a fortnight. The author points out that spontaneous recovery from anuria in Weil's disease may occasionally take place without active treatment. Nevertheless the "close time relation between the induction of high spinal anaesthesia and the start of urinary secretion" in the case reported indicated that the treatment played some part in the recovery.

[This is an interesting paper. It is a pity that full records of urinary output are not available for the period prior to the induction of spinal anaethesia. It might be argued also that the other treatment given, *e.g.*, intravenous plasma and sodium sulphate, might have played a part in the production of diuresis. The reviewer believes, however, from his own experience that the latter explanation is extremely unlikely.] *B. G. Maegraith.*

YAWS.

HACKETT, C. J. **The Clinical Course of Yaws in Lango, Uganda.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 206–17, 35 figs. on 8 pls., 1 map & 2 diagrams. [20 refs.] Discussion 218–27 [WENYON, C. M.; STANNUS, H. S.; FINDLAY, G. M.; WATTS, J. C.; CHESTERMAN, C. C.; HEWER, T. F.; MURGATROYD, F.; BLOSS, J. F. E.; LEECH, R. B.; HACKETT, C. J. (in reply)].

——. **Incidence of Yaws and of Venereal Diseases in Lango (Uganda).** *Brit. Med. J.* 1947, Jan. 18, 88–90.

The material upon which these two papers are based was collected in 1937–40. They are complementary but overlap to some extent and may be considered together.

One of the main points of interest elicited is the interesting comparison between the incidence of yaws and of syphilis respectively in two areas in Uganda. The incidence of yaws at Lira in Lango district was 13 times that at Masaka in Ganda province, while the incidence of syphilis at Masaka was 16 times that at Lira. At Lira the incidence of yaws was 19 times that of syphilis; at Masaka syphilis was 11 times more prevalent than yaws and the yaws cases were largely among immigrants. Yaws cases formed 20 per cent. of 14,707 outpatients at Lira, syphilis 17 per cent. of 16,207 at Masaka. In (ii) tables are given showing the annual out-patient attendances for various groups,

with sex and age distribution and the results of a serological survey. In the first paper (i) the clinical features of the disease are more particularly dealt with, illustrated by a number of excellent photographs of many of the well-known lesions. Dr. Hackett in his summary lays stress upon the following points :—

" The initial lesion may heal before secondary ones appear or may persist into the secondary stage. All other active lesions, apart from a few such as ganglion, hydrarthrosis and goundou, which may occur in more than one stage, are either secondary or tertiary. In many cases secondary lesions cease to relapse 2 to 3 years after infection. In some cases lesions of the secondary type may develop years after the earliest manifestations of infection have healed, while in other cases tertiary lesions may appear within a few years of infection. In many cases there is a more or less symptom-free period of years between the healing of the secondary eruption and the development of tertiary lesions. Lesions of these two types are never observed in the same patient at the same time, nor is the initial lesion present when tertiary lesions have developed."

The paper at the Royal Society of Tropical Medicine and Hygiene was followed by a discussion to which an important contribution was made by Dr. G. M. FINDLAY on yaws in West African populations. *H. S. Stannus.*

SMITH, F. H. **Charcot-like Joints in Yaws.** *U.S. Nav. Med. Bull.* 1946, Dec., v. 46, No. 12, 1832–43, 4 figs. [25 refs.]

STUBENBORD, W. D. **Yaws treated with Penicillin.** *U.S. Nav. Med. Bull.* 1946, Dec., v. 46, No. 12, 1895–8, 2 figs.

Report of a case.

LEPROSY.

GINÉS, A. R. & POLETTI, J. G. La reacción de Mitsuda en los vacunados con BCG. (Posibilidades de la vacunación BCG en la profilaxis de la lepra.) [**Mitsuda's Reaction and BCG Vaccination.**] *Bol. Oficina Sanitaria Panamericana.* 1946, Oct., v. 25, No. 10, 884–8. [English Summary.]

This is an interesting contribution by way of preliminary and is worth following up. FERNANDEZ in 1943 pointed out certain affinities between leprosy and tuberculosis in that positive reactors to tuberculin were positive also to the Mitsuda reaction. From this, the idea naturally followed of the possibility of BCG vaccination being tried as a prophylactic against leprosy. The authors examined 31 boys, some of leprous parents, interned in a sanatorium in Paraguay, but free from leprosy. Twenty-four of them gave positive reactions to tuberculin and some showed infection of the glands by X-rays. All were given BCG by multipuncture (Rosenthal's method). In 11 of them the Mitsuda reaction was not known before the BCG was inoculated, but afterwards 9 were positive. In the other 20 the Mitsuda reaction was negative, but afterwards 16 of them became positive. It is argued that if a positive Mitsuda reaction is a sign of relative immunity to leprosy, then the inoculation of BCG may be able to protect, in some degree at least, against leprosy. [This work was also described in *Hoja Tisiologica*, 1945, v. 5, 287.] *H. Harold Scott.*

HELMINTHIASIS.

MEIRA, J. A. Tratamento das verminoses. [**The Treatment of Worm Infections.**] *Gaz. Clin.* Rio de Janeiro. 1946, May–June, v. 44, Nos. 5/6, 93–121.

OLIVER-GONZÁLEZ, J. **The Possible Rôle of the Guppy,** *Lebistes reticulatus*, **on the Biological Control of** *Schistosomiasis mansoni.* [Correspondence.] *Science.* 1946, Dec. 20, 605.

In Porto Rico, the guppy (*Lebistes reticulatus*) is a fish commonly seen in aquatic regions where the snails *Australorbis glabratus* abound: conversely, when this species of snail is absent, the guppy is usually absent too. Hence it is believed that some element in the snail may constitute an essential food for the guppy.

It was also observed that in certain regions endemic for schistosomiasis, *A. glabratus* could no longer be found, but numerous guppies were seen in the water. When these were studied in laboratory aquaria, they fed actively on egg masses laid by the snails, and also on cercariae shed by them.

Further experiments are being carried out with the object of studying the rôle of the guppy as a "natural enemy" of cercariae-infected snails.

H. J. O'D. Burke-Gaffney.

PINILLA B., C. La distomatosis por *Fasciola hepatica* en el hombre. [*Fasciola hepatica* **Infection in Man.**] *Semana Méd.* Tomo Cincuentenario 1894–1944, Fasc. 2, 585–97. [Numerous refs.]

An historical and medical review.

BACIGALUPO, J., REY, M. & TOCE, A. Teniasis por *Hymenolepis diminuta* en el hombre en la Argentina. [*Hymenolepis diminuta* **Infection in Man in Argentina.**] *Semana Méd.* Tomo Cincuentenario 1894–1944, Fasc. 2, 579–83, 10 figs.

A report of the third case in Argentina.

CANTACUZÈNE, A. & LUPASCO, G. De l'existence d'un important foyer d'ankylostomiase dans les charbonnages d'Anina-Steierdorf. [**An Important Focus of Ancylostomiasis in the Mines of Anina-Steierdorf.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1942, July–Dec., v. 12, Nos. 3/4, 485–94.

Hitherto there have been very few references to ancylostomiasis in Rumanian literature although isolated reports on individual cases have appeared. However, Drs. IBERER in 1903 (*Münch. med. Woch.*, I, 992) reported on the endemic existence of hookworm in Banat. They found a large number of carriers in the Anina coal mines, namely 96 per cent. of 1,647 subjects examined. Although a quarter of the infected persons had symptoms which necessitated hospitalization, they did not consider that these pathological manifestations were entirely due to hookworm infection.

The present enquiry was undertaken to ascertain the number of persons infected amongst the mining population and to investigate what conditions favoured the development of the parasite and the creation of a focus of ancylostomiasis.

The miners consisted of two groups: one of whole-time experienced miners and the other of temporary recruits from the agricultural districts who worked only in the winter season. The latter returned in the summer to the rural districts and were thus possibly a cause of the spreading of the infection.

In the Anina coal mines, the temperature is about 22°C. in the principal galleries but above this figure in the distant workings. There is frequent

flooding. The miners work in very unhygienic conditions ; there are no proper sanitary arrangements so that the soil is contaminated with the faeces of the miners, most of whom work bare-footed. In view of the high temperature, the damp conditions, the contamination of the soil, and the bare-footedness of the miners, highly favourable conditions exist for the development of *Ancylostoma* larvae, for their distribution, and for the infection of the miners.

Stools were examined by Willis' concentration method as modified by HUNG [this *Bulletin*, 1927, v. 24, 195]. Stools of 250, or 25 per cent., of the underground workers were examined during the month of September 1942. The percentage of positive cases was 81, but if more than one stool had been examined for each person it would probably have been higher. It varied in the four different pits of the mine : in two pits, the figures were 96·1 per cent. and 92·3 per cent., while in the other two pits, they were only 70 per cent. and 68·6 per cent.

The results were arranged accordingly to the depth at which the miners were working : this showed a slightly higher percentage in the deepest galleries (980 metres), but the difference was scarcely significant.

No quantitative method of counting the eggs was carried out such as that recommended by STOLL [this *Bulletin*, 1923, v. 20, 949–50] but the numbers of eggs per microscopic field were noted, and are shown in tabular form. The heaviest infections were in the pit that had the highest percentage of positive cases, and the lightest infections in that with the lowest percentage of positive cases.

Many of the miners showed undeniable clinical signs, but of a moderate degree. The clinical signs were digestive troubles, nausea, vomiting, pain in the epigastric region and, occasionally, diarrhoea. Signs of anaemia, with paleness of the mucous membranes, were not infrequent and a few of the men had dyspnoea on exertion.

Blood examinations were carried out in certain cases only ; the red cells were reduced to amounts varying from 3·8 million to 1·9 million per cmm. and the haemoglobin from 60 per cent. to 30 per cent.

Several examinations of the stools of miners' families were carried out, but in 30 cases no positive stools were found. *L. E. Napier.*

JOHNSTONE, R. D. C. **Loiasis.** *Lancet.* 1947, Feb. 15, 250–53.

The main point of interest in this paper lies in the account of personal experiences.

The author became infected with *L. loa* some time between July 1943 and June 1944. In July–August 1944 he noted the gradual onset of a swelling, with pitting oedema, above the right wrist, accompanied by severe neuralgia. This was succeeded by a regular sequence of Calabar swellings. The blood eosinophilia ranged from 12 to 36 per cent.

On the voyage to England in December 1944 there was a noticeable decrease in the number of the swellings to one every third day at most.

Immediately on arrival in England in January 1945, an adult worm was removed from the eye, a second six months later, and after a short interval, a third. This differed from its predecessors by wandering about for some days. At one time it was coiled in the outer aspect of the upper lid and there formed a small Calabar swelling. The emergence of the filaria from the inner canthus was accompanied by the most acute pain. A fourth was removed from the right eye after wandering around for two weeks. Its extraction was slow, necessitating three lamellae of cocaine, which appeared to paralyse it.

Recently there have been no localized Calabar swellings. No microfilariae have been found in the blood throughout. The effect of temperature on the

swellings constitutes an important observation ; they were frequent during the hot summer months, but rare in the cold weather. *Philip Manson-Bahr.*

DEFICIENCY DISEASES.

LEWIS, C. F. & MUSSELMAN, Merle M. **Observations on Pellagra in American Prisoners of War in the Philippines.** *J. Nutrition.* 1946, Nov. 11, v. 32, No. 5, 549–58.

American prisoners of war in the Philippines subsisted on a diet consisting mainly of rice, which provided less than 1,500 calories a day, and was grossly deficient in protein and vitamins. Pellagra broke out after 6 months, and continued to occur throughout the next two years. Eventually almost all the prisoners were affected.

The most severe changes were in the skin. The lesions were more extensive than those usually described in pellagra. They occurred in parts of the body exposed to sunlight, and were aggravated by it. Skin protected by clothing was unaffected, and was sharply demarcated from neighbouring areas of dermatosis. In the affected areas, vesicles and bullae appeared, which often became haemorrhagic and ruptured. This was followed by " weeping ", desquamation, and secondary infection. The slightest trauma resulted in ulceration. The tongue was swollen, raw, and red ; there was inflammation and ulceration of the buccal mucosa, maceration at the corners of the mouth, and seborrhoeic lesions round the alae nasi, lips, and chin. Dermatitis of the scrotum was present in many cases.

Digestive disturbances were common, but in the presence of amoebic and bacillary dysentery it was not possible to distinguish diarrhoea that was specifically a result of pellagra. Many pellagrins were found to have reduced or absent gastric acidity, and the digestive symptoms were relieved by dilute hydrochloric acid. Frequency of micturition, dysuria, and haematuria were also found.

Many patients presented evidence of neurological lesions. Signs of peripheral neuritis responded to treatment with vitamin B_1. In other cases, there was a spastic paresis with exaggerated reflexes. Mental symptoms were mild, and improved with nicotinic acid ; they consisted mainly of irritability, loss of memory, and inability to concentrate. Only a few patients became maniacal or disoriented.

Successful attempts were made to prevent and cure the pellagra by the use of a yeast culture made in the camp. For some months, after the arrival of Red Cross parcels and an increase in the rations issued by the Japanese, there was a substantial rise in the calorie and protein intake. During these months the pellagrins rapidly improved. Severe cases, which did not recover with diet alone, were given nicotinic acid, and a good response was usually obtained with 25–100 mgm. Later, when the Red Cross food was finished and the ration scale was reduced again, nicotinic acid was found to have much less effect in cases of comparable severity. In 1944, a daily issue of one multivitamin capsule, containing 10 mgm. of nicotinic acid, was made to each man ; as a result of this, the severity of the pellagra seemed to be reduced, although the incidence remained high, 25–50 per cent. of the prisoners being affected.

[Pellagra appears to have been more common among the American prisoners in the Philippines than among the British or Australian troops in Singapore and Hong Kong. Detailed figures of the food issued are not given in this paper, so that a precise comparison of the diets is not possible.

This account provides further clinical evidence of the effect of a low protein diet in precipitating pellagra, and of an increased protein intake in helping recovery. It is of interest that when the protein intake was grossly inadequate, the incidence of pellagra remained very high, in spite of a daily supplement of 10 mgm. of nicotinic acid (see MONTEIRO *et al.*, this *Bulletin*, 1947, v. 44, 340).] *J. C. Waterlow.*

PINEDO, C., CÁNEPA, C. H. & FUKELMAN, R. Pelagra y colitis ulcerosa. [**Pellagra and Ulcerative Colitis.**] *Rev. Méd.-Quirúrg. Patol. Femenina.* 1946, July, v. 25, No. 5, 265–8.

Report of a case.

HERNANDO ORDÓÑEZ, J. Melanosis de causa desconocida. Carencia nutritiva, vida en la altura y trastornos hipofisarios como posible causa. [**Melanosis of Unknown Origin. Malnutrition, Life in the Altitude and Pituitary Trouble as Possible Cause.**] *An. Soc. Biol. Bogota.* 1946, July, v. 2, No. 4, 121–46. [Bibliography.] [Summary in English by the author.]

" A peculiar form of melanosis is described, which was found in Bogotá at an altitude of 2,640 meters above sea level in individuals suffering from malnutrition and who have lived for a long time at altitudes between 1,500–2,600 meters* characterized by generalized melanodermia of the skin, nails, conjunctiva, mouth and vulva and organs like lungs, some nervous system centers, the tunica adventitia of the cutaneous arterioles, slight or no asthenia and high or normal blood pressure. This melanodermia disappears or diminishes when patients improve their diet or when treated by sodium chloride, vitamin C or nicotinic acid.

" The cause of this syndrome may be a hypersecretion of the melanotropic hormone of the pituitary stimulated by altitude, or a dietary deficiency of several vitamin or protein factors."

GILLMAN, J. & GILLMAN, T. **The Pathogenesis of Cystiderosis (Hemochromatosis) as evidenced in Malnourished Africans.** *Gastroenterology.* 1947, Jan., v. 8, No. 1, 19–23. [28 refs.]

HAEMATOLOGY.

DAVIS, L. J. **Recent Trends in the Treatment of Megaloblastic Anaemias.** *Glasgow Med. J.* 1947, Jan., v. 28, No. 1, 1–27, 2 coloured figs. on 2 pls. [77 refs.]

SULLIVAN, C. J. & BROUN, G. O. **Avoidance of Allergy to Liver Extract.** *J. Amer. Med. Ass.* 1947, Jan. 18, v. 133, No. 3, 178–9, 1 chart.

" 1. A case of macrocytic anemia with organ-specific allergy to liver extract is reported.

" 2. Administration of folic acid followed later by that of dried stomach and iron solved the serious problem of persistent allergy to liver extract and resulted in maximal and prolonged maturation of erythrocytes.

" Additional note: The blood values after seven months of continuous medication with the same dosage were as follows: red blood cells, 4·25 million; hemoglobin, 12·75 Gm. per hundred cubic centimeters, and mean corpuscular volume, 90 cubic microns."

---

*After I had written this I observed 1 case coming from an altitude of 1,000 meters above sea level.

SPIES, T. D. & STONE, R. E. **Liver Extract, Folic Acid, and Thymine in Pernicious Anaemia and Subacute Combined Degeneration.** *Lancet.* 1947, Feb. 1, 174–6.

The authors have shown, as the result of many years' study, that refined liver products, when injected, produce much more dependable responses than do crude products administered by the mouth.

In order to determine which, if any, of the B-complex vitamins is responsible for the anti-anaemic properties of liver extract the authors have tested many, both singly and in combination, and eventually folic acid was found to produce a definite haemopoietic response in megalocytic anaemia. Later it was demonstrated that 5-methyl uracil (thymine) produced a similar response, though to a lesser degree. The present paper concerns itself with a study of the comparative value of parenteral liver extract, of folic acid and thiamin by the mouth, not only in producing and maintaining satisfactory blood-levels, but in relieving and protecting against neurological disturbances in pernicious anaemia, especially as regards subacute combined degeneration.

It soon became obvious that neurological improvement could not be effected with folic acid. When the disease progressed it was discontinued and 5 cc. of refined liver extract was given daily by intramuscular injection and within 10–12 days there was subjective and objective neurological improvement.

Representative case records are cited.

Four patients with addisonian pernicious anaemia were treated with synthetic thymine in doses of 5–7·5 gm. daily by mouth and this was followed by a satisfactory haemopoietic response, though not so great as with liver or folic acid. Nevertheless increased blood values were maintained throughout the 8 months in which the patients were given 4·5 gm. of thymine daily.

In two patients neurological manifestations progressed rapidly, but regressed on liver-extract therapy.

It is therefore concluded that refined liver extract, administered parenterally in adequate amounts and at suitable intervals, will produce a haematological remission in persons with addisonian pernicious anaemia in relapse, will maintain satisfactory blood-levels and effectively prevent subacute combined degeneration ; but if it is not administered regularly, relapses take place and eventually signs and symptoms of degenerative changes in the nervous system appear ; moreover adequate liver-extract therapy will reverse such changes if not too pronounced. *P. Manson-Bahr.*

BETHELL, F. H., MEYERS, Muriel C., ANDREWS, G. A., SWENDSEID, Marian E., BIRD, O. D. & BROWN, R. A. **Metabolic Function of Pteroylglutamic Acid and its Hexaglutamyl Conjugate. I. Hematologic and Urinary Excretion Studies on Patients with Macrocytic Anemia.** *J. Lab. & Clin. Med.* 1947, Jan., v. 32, No. 1, 3–22. [35 refs.]

SWENDSEID, Marian E., BIRD, O. D., BROWN, R. A. & BETHELL, F. H. **Metabolic Function of Pteroylglutamic Acid and its Hexaglutamyl Conjugate. II. Urinary Excretion Studies on Normal Persons. Effect of a Conjugase Inhibitor.** *J. Lab. & Clin. Med.* 1947, Jan., v. 32, No. 1, 23–7. [15 refs.]

HAYS, E. E. **Effect of Folic Acid upon Primitive Erythrocytes** *in vitro.* *Proc. Soc. Exper. Biol. & Med.* 1946, Dec., v. 63, No. 3, 558–60.

BÉNARD, H., RAMBERT, P., CAJDOS, A. & VAN DEN BROUCKE. L'acide folique dans le traitement des anémies pernicieuses. [**Folic Acid in the Treatment of Severe Anaemias.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 26, 27 & 28, 457–63. [22 refs.]

Report of three successful cases.

VENOMS AND ANTIVENENES.

SERGENT, Et. Scorpions et sérum antiscorpionique. [**Scorpions and Scorpion Antivenene.**] *Bull. Acad. Méd.* 1947, v. 131, Nos. 1/2, 45–9. [Numerous refs.]

In Northern Africa, says the author, scorpion stings cause more fatalities than do snake-bites. As evening approaches they enter dwellings and cling to the walls or hide in clothes. CHAIX, in 1939, recorded 400 cases of scorpion sting, 15 of them fatal. Snake antivenenes are useless in treatment, so in 1935 the author undertook preparation of scorpion antivenene.

There are some 15 species of scorpion in Northern Africa; of these the following are the most important: *Prionurus australis* and *P. liouvillei* in the eastern plains and the Sahara; *P. amoreuxi* and *P. hoggarensis* in the Sahara; *Buthus occitanus* in the hilly districts of Tell and the Sahara; *Hottentota gentilii* in western Sahara, and *Scorpio maurus*, generally distributed.

For experiment, white mice were the best test animals. It is not feasible to obtain the venom itself in sufficient quantity, so the telsons of 100 scorpions of the same species are ground up in 0·9 per cent. saline and glycerin is added. This will retain its toxicity for three years if kept on ice. The relative toxicities of six of the above species were determined in white mice of 20 gm. weight. They were *P. australis* 1/40 telson, *P. amoreuxi* 1/15, *P. hoggarensis* ½, *Buthus occitanus* ½, *Hottentota gentilii*, ¾–1, *Scorpio maurus* 7 telsons. Thus, *P. australis* is the most potent venom and nearly all fatal cases in man have been due to this. Symptoms usually begin to appear between "10 minutes and 10 hours," rarely delayed to 20 and even 24 hours, and when death occurs this is usually 2–20 hours after the infliction of the sting, one-fifth of the fatal cases between 24 and 30 hours. An infant stung has died "in a few minutes." *Buthus occitanus* sting is occasionally fatal in the Algerian littoral area. In some patients the reaction is but slight. This variability is ascribed to the difference in toxicity of the venoms, and to differing susceptibilities of the persons stung (the very young and the aged are more susceptible than the normal adult); also, of course, the scorpion may have expended some of its venoms on someone or something shortly before and the glands, therefore, be partly emptied.

For preparing the antivenene, *P. australis*, the most potent, is used; it proves efficacious against the venoms of the other species also.

Since 1936, 2,209 medical records have been furnished on scorpion stings, some treated by the serum, others not. Grave, desperate cases have numbered 531, of which 134 were *in extremis*; of this total 472, or nearly 89 per cent., were cured. The following are the general rules for dosage: (1) In severe cases, the minimum doses to be injected, subcutaneously or intravenously, as early as possible, for adults 20 cc. (2 ampoules), for children 30–50 cc. (infants are more susceptible to the toxin than are adults). (2) If the onset of symptoms is delayed, do not wait. Late appearance of symptoms may be followed rapidly by death. Also, patients should be kept under observation for several hours, because after a time the symptoms may return and necessitate further administration of antivenene. (3) Generally speaking, the earlier it is given the better; after 4 hours the effect is poor, but recovery has been seen in patients apparently *in extremis* 24 hours after infliction of the injury. Failure is usually attributable to one or other of the following causes: Administration too late, quantity injected too small, surveillance not maintained and the serum in consequence not being repeated in time. [An article of much interest.]

H. Harold Scott.

SERGENT, Et. Sérothérapie antiscorpionique. (Neuvième note.) Observations médicales reçues pendant l'année 1945. [**Treatment of Scorpion Sting by Antivenene. (Ninth Note.) Reports received during 1945.**] *Arch. Inst. Pasteur d'Algérie.* 1946, June, v. 24, No. 2, 112–15.

After a brief narration of the serious symptoms resulting from scorpion stings —coma, pulmonary oedema, priapism, marked fall of temperature, even to 35·7°C.—the author stresses again the necessity for giving adequate doses, of injecting large quantities of physiological saline (up to 500 cc.) and of keeping the patient under observation for some hours in case symptoms return. Though the giving of antivenene should not be delayed, if possible, beyond four hours, it may be efficacious even as late as 24 hours after infliction of the injury.

Giving details of recorded cases in 1945, the author states that four patients with grave symptoms who did not receive the antivenene died ; of 440 who did receive it, 318 were mild and recovered rapidly, 48 had serious but not alarming symptoms and all recovered ; in 74 life was in danger and 13 of these receive special mention. In six, insufficient antiserum was injected ; in two it was given late ; in one both too late and in too small an amount ; in four the symptoms returned and the serum was not repeated.

In summing up, the author refers to the same figures as those given above ; 2,209 reports received ; of this total, 531 were of those whose lives were considered to be in danger and 134 of them *in extremis* ; 472 (88·8 per cent.) were cured. *H. Harold Scott.*

SERGENT, Et. Venin de *Scorpio maurus* L. (=*Heterometrus maurus*). [**The Venom of** *Scorpio maurus*.] *Arch. Inst. Pasteur d'Algérie.* 1946, Sept.–Dec., v. 24, Nos. 3/4, 301–3.

As the author remarks, there are scorpions and scorpions. Some, such as *Prionurus australis*, are able to kill children, and even adults, by their sting ; others, such as *Scorpio maurus* have never been known to cause death. Such differences of potency explain the different opinions that have been expressed regarding the danger of scorpion stings, and, no doubt, have delayed the development of specific serotherapy. At the Pasteur Institute of Algeria, however, the preparation of serum against the dangerous scorpion venoms is now well established, and over 10,000 ampoules were issued for use during the first 10 months of 1946. *Charles Wilcocks.*

DERMATOLOGY AND FUNGUS DISEASES.

SIMONS, R. D. G. P. **Studies on Prickly Heat. Miliaria and Sudamina.** Reprinted from *Dermatologica*. Basel. 1946, v. 93, No. 3, 172–82, 3 figs. [16 refs.]

There is great divergence of opinion on the aetiology, genesis and pathology of prickly heat.

"Briefly the main theories are that :—

"(1) it is an eczema (JADASSOHN) ;

"(2) it is a pyodermia (DARIER) or a mycotic infection occurring on the skin previously macerated by sweat (SMITH, Lagos, etc.) ;

"(3) prickly heat is a disease primarily of the sweatglands and every infection is secondary (COATS, POLLITZER, LESSER, etc.) ;

"(4) prickly heat is not a disease of the sweatglands (TÖRÖK, VOLK) but of the sebaceous glands (UNNA)."

The author suggests that the malady is a "partial" eczema characterized by an erythemato-papular-bullous eruption.

He considers it unlikely that the eruption is caused by pathogenic organisms. He suggests that the principal aetiological factor is an increase in sweating and that smallness of the external openings of the ducts of the sweat glands is the vital cause.

Owing to this smallness, the sweat accumulates in and distends the glands Localized inflammatory irritation is caused. Prickly heat rarely occurs in the axillae because the sweat glands of these areas are large.

Simons suggests that *miliariasis erythematosa et papulosa tropica* is a preferable name for the malady.

He makes an interesting reference to a white leprous patient, 20 years of age, who failed to develop prickly heat on anidrotic areas of his skin, although surrounding areas showed the lesions.

He suggests, for therapy, painting the parts with a buffered sulphur lotion, viz. :—

Acid phosphoric	2	(buffer)
Sodium hydrox.	½	(buffer)
Sulph. precip.	20	(antiseptic)
Zinci oxidi	20	(excipient)
Glycerin	10	(excipient)
Spirit 50 per cent. ad	100	(disinfectant and cool constituent)

If required, menthol, camphor or carbolic acid (½ to 1 per cent.) with or without citrus oil (this last as a perfume) can be added.

"The reaction of this lotion must be neutral or slightly acid to litmus. If it is too acid it will cause irritation." *R. M. B. MacKenna.*

CATANEI, A. Nouvelles observations sur les teignes en Algérie et dans les colonies françaises. [**Further Observations on Ringworm in Algeria and the French Colonies.**] *Arch. Inst. Pasteur d'Algérie.* 1946, June, v. 24, No. 2, 116–21.

In 1936 the author published the results of an investigation undertaken during the preceding ten years concerning ringworm infections in Algiers [this *Bulletin*, 1938, v. 35, 91]. During the ensuing ten years he has had an opportunity to examine many schoolchildren of that city. A total of 660 of these were found to have trichophytosis ; 58 were Europeans (30 boys and 28 girls) and 602 were Mohammedans (391 boys and 211 girls). Over 70 per cent. of the European children presented lesions caused by *Tr. glabrum* and in 10 per cent. the lesions were due to *Tr. violaceum*. *Tr. acuminatum*, *Tr. fumatum*, *Tr. crateriforme* and *Tr. plicatile* were demonstrated in other cases. In the Mohammedan children, approximately the same percentage were infected with *Tr. glabrum* and 25 per cent. with *Tr. violaceum* ; *Tr. acuminatum* and *Tr. fumatum* were each isolated in three cases, whilst *Tr. regulare* and *Tr. plicatile* were each inculpated in one case.

The author claims that the trichophyta which have infected children in Algiers from 1926 to 1946 are now known. During this period *Tr. glabrum* was isolated four times more frequently than *Tr. violaceum* in the Europeans, and three times more frequently in Mohammedans.

Only thirty new cases of microsporosis have been revealed during the last ten years ; sixteen of these have been Europeans (12 boys, 4 girls) and 14 Mohammedans (11 boys, 3 girls). All were due to *M. canis*. This form of microsporosis is relatively rare ; only 40 cases have been discovered since 1926 in a total of 997 children with fungous infections.

Since 1936, favus has been diagnosed in 61 children (10 Europeans, 51 Mohammedans: 50 boys, 11 girls). All were due to *Achorion schönleini*.

The author discusses briefly the types of fungi isolated from cases of ringworm in various French Colonies, including Madagascar, and refers also to infections in adults and children caused by *Ctenomyces mentagrophytes*.

R. M. B. MacKenna.

BYRNE, E. A. J. **Effect of Organic Mercurial Preparations on Diseases of the Skin.** *Brit. Med. J.* 1947, Jan. 18, 90–92. [13 refs.]

This is a report concerning the treatment of 500 cases of skin disease in the tropics with organic mercurial compounds. The compounds used were phenyl mercuric chloride, acetate and benzoate: the first of these was regarded as preferable, for the acetate and benzoate have a marked affinity for chlorine and, in the opinion of the author, are likely to be converted to phenyl mercuric chloride when in contact with tissue fluids.

Four types of application were used, the first two being loaded with phenyl mercuric chloride—an ointment made with eucerin and distilled water; a calamine lotion in which the compound was precipitated on the calamine: 0·5 per cent. phenyl mercuric chloride calamine powder; an aqueous solution of phenyl mercuric acetate 1/8,000. Instructions concerning the preparation of these applications are given in the paper.

The reaction velocity of phenyl mercuric chloride depends on the concentration applied, and the duration of the application.

The ointment, therefore, is best applied on lint which is bandaged on to the affected part for a fixed period. It is claimed that 3–4 hours' application of 0·125 per cent. strength was sufficient to overcome the infection in all cases of tinea cruris, corporis, and capitis. For about 24 hours after the treatment the skin was lightly red and itching; then the lesion began to fade and in 5 to 6 days the skin became normal, though some slight desquamation usually occurred. In a few resistant cases a second application of 0·2 per cent. strength was used for three hours.

A total of 200 cases of ringworm of the trunk and limbs, 110 of *Epidermophyton inguinale* infection, 90 of epidermophytosis of the feet, 50 of "jungle sores", and 50 of infected wounds of various types were successfully treated.

Epidermophytosis of the feet was treated with the powder, if the lesions were moist, and with the ointment (0·125 per cent. strength) when dry. Socks may be steeped for an hour in 1/20,000 phenyl mercuric acetate solution before being washed: boots and shoes may be sponged with 1/2,000 alcoholic solution of the same compound.

The author discusses the treatment of jungle sores and dhobi itch; also the toxicology of organic mercurical compounds and their mode of action when used for therapeutic purposes.

R. M. B. MacKenna.

No. 720
1946

SMITH, C. E., BEARD, R. R., ROSENBERGER, H. G. & WHITING, E. G. **Effect of Season and Dust Control on Coccidioidomycosis.** *J. Amer. Med. Ass.* 1946, Dec. 7, v. 132, No. 14, 833–8, 4 figs. [Refs. in footnotes.]

An intensive epidemiological investigation, based chiefly on the test of skin sensitivity to coccidioidin, was conducted in connexion with the Army Air Fields in the San Joaquin Valley, California, a notorious endemic area of coccidioidomycosis. Routine skin testing was carried out on all new arrivals at the air stations, and the coccidioidin-negative subjects were re-tested at intervals to detect new coccidioidal infections: the coccidioidin-positive reactors were considered to be immune, and none of these developed the

clinical disease. As a result of repeated re-testing of the "susceptibles" it became evident that the proportion of completely inapparent or asymptomatic coccidioidal infections exceeded that of the clinically recognizable disease.

It is generally accepted that the wind-borne desert dust contaminated by the spores of *Coccidioides immitis* is the vehicle of infection and the path of entry is through the lungs by inhalation. Heavy rainfall in the winter, by aiding the vegetation of *C. immitis* in the desert soil, usually causes a high incidence of infection in the succeeding dry season, but rain in the hot, dry season, by laying the dust, reduces the rate of infection. The construction of air fields, which involved much excavation and levelling with consequent dust clouds, was associated with a high rate of infection, but a notable reduction occurred when the bare earth was converted into grass lawns and the roads and runways were given a hard surface. Athletic grounds and playing fields presented a dust problem which was dealt with by oil-spraying. Thick, crude oil was found unsuitable, but a refined oil proved very effective on permeable clay soils, although not on a soil composed of the fine silt of a former lake bed. The use of swimming pools as an alternative to dry land games is recommended. No solution has been found to the problem of wind-borne dust from remote points.

J. T. Duncan.

SILVA, M. S. Blastomicose pulmonar (paracoccidioidose pulmonar). [**Pulmonary Blastomycosis (Paracoccidioidosis).**] *Rev. Brasileira Med.* Rio de Janeiro. 1946, Sept., v. 3, No. 9, 723–31, 9 figs.

The first half of this paper is taken up with a discussion of the classification and nomenclature of the causative fungus in this condition. The majority of those attacked have some agricultural occupation, or are working in contact with the soil. Cutaneous, mucous, glandular and visceral localizations are said to be uncommon, but that is probably due to the fact that the lesion present is not diagnosed early, often not before pulmonary lesions have been set up; in fact, X-ray examination of the lungs may first put the physician on the track of correct diagnosis. Radiologically, the findings differ from those of pulmonary tuberculosis in being more extensive, nearly always bilateral and symmetrical and rarely showing cavity-formation. It is commonly said that pulmonary blastomycosis has no symptoms; this is erroneous. There is nearly always cough and expectoration, dyspnoea of greater or less intensity, rise of temperature and night sweats. Diagnosis is difficult without sputum examination, but would be more often made if such examination was carried out in all those with unexplained lung symptoms. Buccal or oropharyngeal and laryngeal symptoms precede the pulmonary (yet another point differentiating it from tuberculosis). Photographs illustrate the lesions of the lips, mouth and tongue, and X-ray reproductions the pulmonary signs. Treatment by sulphonamides in the early stages proves fairly satisfactory and may lead to clinical cure, but if treatment is postponed the outlook is bad. Penicillin has wrought no benefit.

H. Harold Scott.

MISCELLANEOUS DISEASES.

FAIRLEY, N. H. **Wartime Research on Malaria and other Tropical Diseases of Military Significance.** *The Fight against Disease.* Research Defence Society, London. 1947, v. 35, No. 1, 2–19. [19 refs.]

An informative review of work on malaria, dengue, dysentery and typhus.

D'ABRERA, V. St. E. **Further Observations on Cases of Asthma and Bronchitis associated with High Eosinophilia and with Mites in the Sputum.** *Indian Med. Gaz.* 1946, Oct., v. 86, No. 10, 414–17. [10 refs.]

GELFAND, M. **Idiopathic Thrombophlebitis.** *Clin. Proc.* Cape Town. 1946, Nov., v. 5, No. 9, 381–7, 3 figs.

The author describes the clinical features observed in 15 cases of idiopathic thrombophlebitis seen by him at Salisbury, Southern Rhodesia. He admits that the aetiology is obscure, and has found no relationship with the Weil-Felix reaction or the platelet count. In all his cases there was pain over the affected vein, and usually fever ; the duration of the acute phase varied from a few days to several weeks. Polymorphonuclear leucocytosis was usually found, and the white cell count was generally 10,000 to 15,000, but sometimes higher. [MANSON-BAHR and CHARTERS (this *Bulletin*, 1946, v. 43, 1186) found little change in the leucocyte count, other than relative lymphocytosis in a few cases.] An outstanding feature of the disease, if it affects the principal vein of a limb, is the oedema of the limb distal to the thrombus.

The author notes that thrombosis usually affects only a small portion of the vein, and that it does not usually spread, though occasionally it may do so. He gives details of one patient in whom the thrombosis spread from the external jugular vein to the subclavian and axillary veins. Emboli are rare, but the author has seen one case.

If the mesenteric or portal veins are involved, the clinical picture is that of an acute abdominal condition, and the prognosis may be very grave. At operation, gangrenous bowel may be found, and a case is described in which three feet of small intestine were removed for this condition, with complete success. " Portal thrombosis is usually rapidly fatal. The chief symptoms are pain, haematemesis and collapse." *Charles Wilcocks.*

SAGHER, F. **Tropical and Phagedenic Ulcer and Desert Sore. A Review.** *Acta Med. Orientalia.* 1946, Dec., v. 5, No. 12, 405–12. [101 refs.]

A review of the literature.

D'IGNAZIO, C. & CODELEONCINI, E. Sul reperto di forme Rickettsiose nel pus poradenitico. [**Rickettsial Forms found in Pus from Cases of Poradenitis.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1946, v. 6, No. 5, 243–52. [11 refs.]

The authors have inoculated pus intracranially, the material being taken from cases of Nicolas-Favre disease, into certain laboratory animals, white mice, guineapigs and rabbits ; and also by Weigl's method they inoculated lice with a culture of the virus. In the last they found Rickettsiae in about 60 per cent. of one group and 33 per cent. of another, 30–50 in a field, always in small masses. *H. Harold Scott.*

KATZENELLENBOGEN, I. **Granuloma Venereum in Palestine.** *Acta Med. Orientalia.* 1946, Dec., v. 5, No. 12, 391–9, 5 figs. [34 refs.]

A survey of 12 cases.

CORCORAN, A. C. & PAGE, I. H. **Renal Damage from Ferroheme Pigments Myoglobin, Hemoglobin, Hematin.** *Texas Reports on Biol. & Med.* 1945, v. 3, No. 4, 528–44, 3 figs. [29 refs.]

This paper records the results of experiments designed to determine the degree and nature of the renal injury resulting from myoglobinuria. The

experiments were conducted in dogs whose urine was acidified by administration of a diet rich in casein and meat, supplemented by sodium acid phosphate. Renal function was estimated by diodrast and inulin clearances. Myoglobin (in the meta-form) was prepared from beef heart muscle. The pigment was made up in physiological saline and sterilized by filtration. It was injected intravenously into unanaesthetized trained dogs. The dosage was calculated to correspond roughly to the amount of myoglobin liberated in human beings following crush injury to the leg and thigh. Parallel experiments were carried out involving the intravenous injection of haemoglobin from lysed red cells of dogs and of sodium ferrihaemate.

Myoglobin and metamyoglobin were injected into nine dogs (excluding an experiment in which the pigment was not sterile) and oxy- and reduced forms of the pigment into two. The immediate effects of injection varied. There was an increase of diodrast clearance in five animals, associated in three with normal inulin clearance and lowered tubular secretory capacity for diodrast and in two with lowered inulin clearance (one with normal, the other with lowered tubular secretory capacity). In one animal the diodrast clearance was normal and inulin clearance and tubular secretory capacity reduced. In all other animals, except one in which measurements are not recorded, diodrast and inulin clearances and tubular secretory capacity were lowered.

The subsequent effects of the pigment injections can be seen by inspecting the table.

The degree of renal damage as estimated from " percentile changes in tubular secretory capacity " were found to be roughly proportional to the amount of pigment retained by the body ; the amount retained was not a function of the urinary *p*H.

The effects of injection of haemoglobin were similar to those of injection of myoglobin. Injection of sodium ferrihaemate proved nephrotoxic above a certain level of dosage.

After an interesting discussion, the authors conclude from their experimental results that intravenous injection of aciduric conscious dogs causes " partially recoverable renal injury of varying degree." They consider, therefore, that myoglobinuria may be a significant factor in the pathogenesis of renal damage in the crush syndrome. They qualify this conclusion, however, in the light of certain experiments (unpublished) in which they were unable to obtain renal failure of " uremic degree " in normally hydrated aciduric rats following injection of myoglobin, whereas similar doses of myoglobin in dehydrated rats with crushed limbs often resulted in renal damage. Thus other renal functional changes in addition to aciduria, such as oliguria, high urinary salt concentration, ischaemia and functional renal tubular injury may determine the renal damage caused by circulating myoglobin. The authors consider that renal tubular obstruction may result from precipitation of pigment and such obstruction may account for the decrease of glomerular filtration observed (expressed presumably as inulin clearance). The initial maintenance of diodrast clearance following injection of the pigment must therefore be evidence of renal hyperaemia. " That renal hyperaemia is present is borne out by the increased diodrast clearances present in five of ten observations. The occurrence of renal hyperaemia during injections of myoglobin or haemoglobin contrasts with oncometric observations . . . of decreased kidney volume during haemoglobin infusion and vitiates the supposition that haemoglobinuric renal injury is primarily ischaemic."

The general reduction of estimated renal function in the other experimental animals at the time of injection is not discussed.

The authors conclude that the renal injury in aciduric myoglobinuric dogs results from (i) tubular obstruction by pigment, (ii) impaired tubular secretory

TABLE

Effects of Metamyoglobin, Myoglobin and Haemoglobin Injection on Renal Function in Dogs.

Dog No.	Urine *p*H	Urine cc./min.	Injected mg./kg.	Retained mg./kg.	C_D	Percentage Normal			2 days C_1	Tm_D	Renal Function		
						Immed. C_1	Tm_D	C_D			C_D	2 weeks C_1	Tm_D
						Metamyoglobin							
21–93	6·5	1·2	88	—	—	—	9	—	—	11	—	—	4
15–67	6·0	0·8	78	21	76	59	74	78	57	29	76	77	66
15–79	5·6	0·7	64	14	101	64	61	72	80	80	97	93	90
15–62	5·8	0·1	146	114	7	8	7	24	18	17	74	66	80
16–38	5·6	0·2	189	39	—	—	—	113	119	90	94	117	86
16–54	5·8	0·2	215	65	142	105	48	81	95	61	88	74	96
15–86	5·3	0·4	208	78	118	52	27	123	80	66	86	77	66
16–74	5·8	1·0	252	97	138	107	30	104	103	58	136	80	67
16–04	5·1	1·2	100	25	142	107	94	85	84	58	93	92	74
15–66	5·9	0·8	101	37	71	45	34	78	61	35	81	82	72
						Myoglobin							
16–21	5·7	1·0	75	14	121	84	76	78	90	70	119	109	68
16–29	5·75	0·8	180	62	58	65	36	54	45	43	83	87	100
Mean	5·66	0·7	136	51	97	72	49	81	75	55	84	86	78
						Haemoglobin							
15–67	5·5	0·5	190	—	99	96	74	90	68	96	75	69	98
15–79	5·7	0·4	655	—	67	40	43	42	32	29	60	67	83
16–04	6·5	0·6	582	—	89	95	100	110	75	104	110	88	—

Legend: Urine *p*H and volume as measured at the time of pigment injection. Changes in renal function (C_D equals plasma diodrast clearance, C_1 equals plasma inulin clearance, Tm_D equals tubular secretory capacity for diodrast) are expressed as percent. of control levels. The final observations of function were most commonly made at two weeks or more after pigment injection. The mean of metamyoglobin and myoglobin experiments is the arithmetic mean of the series, but does not include the experiment on Dog No. 21–93 in which the metamyoglobin given was not sterile.

activity arising from ingestion of pigment by the epithelial cells, and (iii) cytotoxic activity of haematin liberated within the tubules.

[The authors dismiss too lightly the oncometric observations of other workers on renal volume changes following infusion of blood pigments. The increased diodrast clearances observed immediately after injection of metamyoglobin and myoglobin in five animals may be interpreted as evidence of increased total renal plasma flow and therefore of hyperaemia, but such increased intrarenal flow is not necessarily incompatible with the reduction in renal volume. It is possible, for instance, that in these animals the *rate* of flow through certain parts of the kidney was increased (*e.g.*, by the opening up of arterio-venous shunts) sufficiently to increase the total blood flow. Further, it will be seen from the table that in four other animals the injection of pigment was associated with reduction in diodrast clearance, indicating a reduction in total renal plasma flow, which is, of course, consistent with a diminution of renal volume.

In the experiments in which the immediate effect of pigment injection was noted, diodrast clearances were increased in five animals, decreased in four and unchanged in one. In two animals the inulin and diodrast clearances were reduced proportionately, but in eight the inulin clearance was reduced by 20 to 40 per cent. more than the diodrast clearance. These results could be interpreted as indicating that in the latter eight animals a differential redistribution of blood flow had occurred whereby the glomerular vascular beds received relatively less blood than the rest of the kidney. This possibility does not seem to have struck the authors. In the reviewer's opinion, this interpretation of the results alters the whole argument.] *B. G. Maegraith.*

GENERAL ENTOMOLOGY.

MER, G., BIRNBAUM, D. & AIOUB, A. **The Attraction of Mosquitoes by Human Beings. Statistical Analysis of Data by** R. BACHI. *Parasitology.* 1947, Jan., v. 38, Nos. 1/2, 1–9.

The authors are interested in factors which attract a female mosquito to man. They realize that in nature there may be a long-range attraction, for instance from the marsh to the village, and that quite different factors may guide the mosquito over short distances, as, for example, when it flies across the room. They limit themselves to the short-range phenomenon which is studied in the laboratory.

The work has been done with a cage 180 cm. long × 60 × 60 cm. wide and high [presumably it is made of mosquito netting or wire screening]. A transverse partition can be inserted across the cage cutting off a length of 20 cm. at either end. With this it is shown that mosquitoes tend to settle near the ends in numbers which are disproportionately great.

In carrying out an experiment, hungry female *Anopheles elutus* are liberated in the cage and left to settle down. A man is then put as bait outside the end of the cage and the numbers of mosquitoes in different parts of the cage recorded after fifteen minutes. In the first set of twelve experiments, the man sat facing the cage and no precautions were taken to remove any influence which his breath might have upon the mosquitoes: he sat with his head and chest on a level with the cage at a distance of 30 cm. from the end of it. Adding up the

result of twelve similar experiments it was found that 566 mosquitoes had been used, and that when there was no human being present 83 of them occurred in the end compartment which could be shut off by the partition. When, however, the human subject was present an average of 264 occurred in that compartment. From these figures the authors calculate an index of attraction :—

$$\frac{264-83}{566-83}=37{\cdot}4 \text{ (per cent.)}$$

In other experiments the man sat with his back to the cage or his breath was led away down a pipe and delivered outside the room : in these the index of attraction was nil. In another group of experiments the subject's breath was led away but a fan played over his body and towards the cage : the index was 29. [In this case the authors do not seem to have considered whether the mosquitoes were moving towards a gentle wind or towards the human being.] In another series of experiments the volunteer sat outside the room but his breath was brought in by tube and delivered opposite the end of the cage ; the index of attraction was 40. Experiments were also carried out in which the cage was slung vertically over the head of the seated subject.

The authors' conclusions, which are supported by a large amount of experimental work, critically analysed from a statistical point of view, are :—

1. The air expired by the human being attracts mosquitoes.
2. It is not only the expired air which attracts mosquitoes but also other substances emanating from the surface of the human body (though probably with less intensity).
3. In the absence of a horizontal air movement the attraction is exerted in a vertical direction, perhaps because of the column of warm air rising from the man's body.
4. Hungry female *A. elutus* are attracted to the human being, in short experiments (15 min.) from a distance up to 330 cm. (say 11 ft.).

The experiments are essentially simple and the details well thought out. The results have been critically considered with reference to statistical questions. The paper is one that should be studied in the original. *P. A. Buxton.*

KING, W. V. & HOOGSTRAAL, H. **Three New Anopheline Records from New Guinea.** *J. National Malaria Soc.* 1946, June, v. 5, No. 2, 153–6.

A female anopheline taken in January 1945 from a large rain forest clearing 2 miles east of Lake Sentani, northern New Guinea, proved to be *Anopheles karwari*. Larvae of this species were taken during March to May 1945 in considerable numbers at Hollandia, in a treeless, grassy bog, and in wheel-ruts and shell-holes with a few larvae of *A. farauti* and *A. punctulatus*. Larvae of *Culex whitmorei*, *C. halifaxi*, *C. pullus* and a species of the *C. vishnui* group were also taken. From March to June, adults of *A. karwari* were common in tents after dark but were rarely seen in the daytime. The females bite quite readily but the species is not regarded as a vector of malaria ; 119 females were dissected but none was found infected.

Larvae of *A. lungae* were also taken at Hollandia ; they were found in muddy hog-wallows with larvae of a species of *Aëdes*, *Bironella gracilis* and a species of *Culex*. There were no adults in the houses though *A. punctulatus* and *A. farauti* and intermediate forms were common.

One female anopheline taken in April 1945 may prove to be the new species *Anopheles clowi*. *H. S. Leeson.*

FEDOROV, V. G. [**Detection of** *Culex molestus* **Forskal in Leningrad.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 2, 58–68, 3 figs. [Numerous refs.] [In Russian.]

The author notes the occurrence in Leningrad of a culicine mosquito which was responsible for mass attacks on human beings during the autumn and winter months. Their breeding places were cellars, the temperature of which was considerably higher than that in the open. At first this mosquito was identified as *Culex pipiens pipiens*, but a thorough study of its morphological characters and bionomics revealed features characteristic of *C. p. molestus*. Like the last-named species it readily attacks man and feeds on his blood, it copulates in restricted spaces (stenogamy), lays eggs without a preliminary blood meal (autogenicity), does not enter the imaginal diapause, and the females do not fatten towards winter. *C. A. Hoare.*

DAVID, W. A. L. & BRACEY, P. **Factors influencing the Interaction of Insecticidal Mists and Flying Insects. Part IV. Some Experiments with Adjuvants.** *Bull. Entom. Res.* 1947, Jan., v. 37, Pt. 3, 393–8, 2 figs.

The yellow fever mosquito *Aëdes aegypti* was employed in experiments to study the mode of action of adjuvants which are added to pyrethrum sprays to enhance their effects. It was noted that with the addition of two common adjuvants, IN930 (isobutyl undecyleneamide) or Sesame oil, the " knockdown " of the insects was appreciably delayed.

From earlier experiments (DAVID & BRACEY, 1944, *Nature*, May 13, 594) it was known that a part of the effect of these adjuvants was due to their physical effect on the spray droplets. Evaporation was delayed and the larger drops resulting impinged on the insects more readily. Experiments were undertaken to see if the residual enhancement of toxicity could be explained by any such physical action on the spray droplets. It was found that their effect is not due to increasing the dose accumulated by the insect but to some unexplained action on the toxicity of pyrethrins. No synergistic action could be obtained with these adjuvants and the insecticide DDT. *J. R. Busvine.*

MADDEN, A. H., SCHROEDER, H. O., KNIPLING, E. F. & LINDQUIST, A. W. **A Modified Aerosol Formula for Use against Mosquitoes and Houseflies.** *J. Econom. Entom.* 1946, Oct., v. 39, No. 5, 620–23.

The authors propose to use " motor oil " [? lubricating oil] to enhance the insecticidal effect of DDT-pyrethrum aerosol. It is suggested that the cyclohexanone content be reduced from 10 per cent. because it is liable to damage lacquers and plastics if the aerosol be used carelessly. The finally approved formula is :—DDT, 3 per cent. ; motor oil, 5 per cent. (viscosity not important) ; pyrethrins 0·3 per cent. ; to be dispersed by *Freon*. *J. R. Busvine.*

RICE, R. I., JOHNSTONE, H. F. & KEARNS, C. W. **A Simple Exhaust Aerosol or Spray Generator for dispersing Insecticide Solutions.** *J. Econom. Entom.* 1946, Oct., v. 39, No. 5, 652–8, 4 figs.

This is a technical description of an exhaust generator for fitting to internal combustion engines for the dispersal of insecticides ; it has been used successfully against flies and mosquitoes both inside buildings and outdoors, and against mosquito breeding places and certain insect pests of crops.

The equipment was originally designed for fitting to a " jeep " for DDT spraying but it can be adapted to other internal combustion engines on heavy trucks, motor-boats and light aeroplanes and for use with other insecticides.

The authors discuss the theory of this method of insecticide dispersion and describe their experiments for its perfection, the installation of the device on different motor vehicles and light aeroplanes and the methods of its operation.

The subject is illustrated by drawings of the details of construction and by photographs and there are tables of figures showing the performance of the generator on the exhausts of a " jeep " and an aeroplane ; and the dimensions of the exhaust aerosol generators necessary for different sizes of engines.

H. S. Leeson.

SYMES, C. B. & HADAWAY, A. B. **Initial Experiments in the Use of DDT against Mosquitos in British Guiana.** *Bull. Entom. Res.* 1947, Jan., v. 37, Pt. 3, 399–430, 3 plans & 6 figs. on 1 pl.

See this *Bulletin*, 1945, v. 42, 785.

JOHNSON, C. G. **Lethane 384 on Clothing as a Mosquito Repellent.** [Memoranda.] *Brit. Med. J.* 1947, Jan. 18, 92–3.

The insecticide Lethane 384 (50 per cent. *Beta*-butoxy *Beta*-thiocyano-diethyl ether in odourless kerosene) has a certain value as a mosquito repellent on clothing when dimethyl phthalate is unprocurable or cannot be used because of its action on plastic materials. Lethane is not suitable to apply to skin because of its irritant and toxic properties.

Experiments showed that about 4 cc. sprayed over thin cotton stockings had a definite protective effect (nearly 90 per cent.) from bites of various mosquitoes (*Aëdes* spp. and *Anopheles claviger*) in Surrey for a period of five hours after spraying. If the stockings were removed and rolled up, the effect was lost by next morning.

A general spraying of the outer clothing could not be relied upon, however, to give protection to uncovered skin of the face and forearms. *J. R. Busvine.*

WHARTON, G. W. **Observations on** *Ascoschöngastia indica* **(Hirst 1915) (Acarinida ; Trombiculidae).** Reprinted from *Ecological Monographs.* 1946, July, v. 16, 151–84, 24 figs. [33 refs.]

There are still many gaps in our knowledge of the morphology and behaviour of the trombiculid mites which carry scrub typhus, and their near relatives. This paper is the most thorough account which has yet been published of such a mite.

Ascoschöngastia indica (commonly called *Neoschöngastia indica* in the literature) has not itself been incriminated as a vector of *Rickettsia tsutsugamushi*, but it closely resembles the mites which have and is itself of interest as being one of the species of mite having been recorded from India, the Dutch East Indies, Ceylon, the Maldive Islands, the Philippines, and the South-West Pacific generally. Its larva stage is a parasite of rats and other small mammals.

A full and accurate account of the morphology describes the egg, the deutovum in which the developed larva remains resting inside the ruptured egg shell, the larva, the nymphochrysalis during which the larva metamorphoses to the nymph, the imagochrysalis (resting stage between the nymph and adult), and finally the adult.

Clear and accurate drawings indicate the essential morphological features of all the stages and it is satisfactory to find diagrams showing the whole animals and not restricted solely to small diagnostic features. Other workers will be able to use this as a foundation on which to base a more satisfactory description of some of the other species.

The section on the biology of the mites is of considerable interest, but is less satisfactory as the author admits that no really successful method of rearing "mass" cultures has been developed.

Nymph and adult appear to be carnivorous, and in captivity often cannibalistic, and they will feed on their own eggs. It has been possible to rear individual mites through from engorged larvae removed from wild rodents to the adult stage but the number is very small. Again, difficulty has been obtained in persuading the unengorged larvae to attach themselves to the host.

There is a full ecological account of the territory in the Island of Guam in the Marianas Islands where this work was done. Some account of the relation between the host vertebrates, parasites and the vegetation is given. On this Island, the species *Rattus mindanensis* was the host for the larvae. It is interesting to note that they were found to remain attached for as long as 32 days, which is a much longer period that has been described for some other species of trombiculid. *Kenneth Mellanby.*

LABORATORY PROCEDURES.

BHATTACHARJI, L. M., SINGH, J. & SEN GUPTA, G. P. **A Simple Methylene Blue-Eosin Substitute for Leishman and Giemsa Stains.** *Indian Med. Gaz.* 1946, Oct., v. 81, No. 10, 400–401.

In 1924, PROESCHER and KRUEGER [this *Bulletin*, 1925, v. 22, 304] described the preparation of a polychrome methylene blue by means of employing strong oxidizing agents as accelerators.

Owing to the shortage in India, during the war, of materials for preparing the common modification of the Romanowsky stain, the authors set out to provide a substitute which could be easily and rapidly prepared with materials available in India.

Many experiments were made with the use of different concentrations of dyes and oxidizing agents, which would readily produce all the effects of metachromatic staining; the following formula was finally adopted as the most satisfactory one :—

Methylene blue (medicinal B.P.)	1·0 gm.
Potassium permanganate (medicinal)	0·3 gm.
Water-soluble yellow eosin (B.D.H., London)	0·4 gm.
Water, distilled or tap	250 cc.

The preparation of the stain is described in great detail in the original paper: but, briefly, the steps are as follows :—

(1) The 250 cc. quantity of water is divided into 3 parts, namely 100 cc., 100 cc. and 50 cc.

(2) In one lot of 100 cc., there is dissolved 1·0 gm. of methylene blue: in the second lot of 100 cc. 0·3 gm. of potassium permanganate is dissolved. Slightly alkaline tap water, *p*H 7·2 to 7·6 is satisfactory.

(3) The methylene blue solution is heated in a porcelain dish over a direct flame, and is allowed to steam (but not to boil) for about 5 minutes.

(4) To this steaming blue solution, the potassium permanganate solution is added gradually. A fine layer of crystals forms on the surface. Heating is continued for about 10 minutes.

(5) In the remaining 50 cc. of water, 0·4 gm. of eosin is dissolved and added to the steaming methylene-blue permanganate mixture, and the contents mixed well by stirring. A thick yellow scum appears on the surface.

(6) Heating is continued for an hour or longer, until evaporation is complete, when a thick scum with a metallic lustre is left. The mixture should not be heated too strongly.

(7) The residue is left overnight in a desiccator or a 37°C. incubator: when it is dry, the scum peels off in shining green flakes, or may be removed with a scalpel. This residue is powdered in a dry glass mortar and stored in a dry airtight glass container.

For use as a substitute for Leishman stain, 0·1 gm. of the powder is dissolved by grinding in 40 cc. methyl alcohol. If solution is complete, filtering is not required. Solutions have been shown to keep for months, with excellent results.

When a substitute for Giemsa stain is required, 0·3 gm. of the powder is ground in a mixture of 25 cc. each of glycerine and methyl alcohol, added very gradually. The solution is allowed to remain at room temperature in a glass bottle overnight. Next day, the bottle is placed in a water bath, neck deep, for about two hours [temperature not stated].

In each case, the technique of staining blood smears is identical with that followed in the original Leishman or Giemsa method.

H. J. O'D. Burke-Gaffney.

LANGE, H. F. Takata's reaksjon ved ekstrahepatiske lidelser. [**Takata's Reaction in Extrahepatic Lesions.**] *Nordisk Med.* 1947, Feb. 14, v. 33, No. 7, 432–4. [Summary in English by the author.]

" After extensive use of Takata's reaction the author has found it suitable as a general protein test. Out of 123 cases of positive reaction 73 (about three fifths) occurred in extra-hepatic lesions, especially in chronic, non-specific affections of the lungs. Positive Takata reaction is also in pulmonary diseases an unfavourable prognostic sign."

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

ROSS INSTITUTE OF TROPICAL HYGIENE. INDIA BRANCH. Royal Exchange, Calcutta. **Report of the Committee of Control for the Year ended 31st July, 1946** [BANNERMAN, H. C., Chairman]. pp. 5+64, 2 pls. & 1 chart.

This report gives a precise and interesting account of the achievements of the India Branch of the Ross Institute of Tropical Hygiene since its inauguration in 1930 under the direction of its Principal, Dr. G. C. RAMSAY, who has recently retired. The Branch has made very important contributions to the health and welfare of tea estates in Assam and Northern Bengal, of tea, rubber, coffee and cardamom estates in Southern India and of numerous other industrial interests in various parts of India. Although the study of malaria and antimalaria measures have been the chief preoccupation, other important health problems have not been neglected. The effects of the war on tea estates in North-East India are described, as are recent advances in antimalaria work. Altogether it is a record of which the Branch may be justifiably proud.

Norman White.

O'BRIEN, T. P. **The Methods and Aims of a Race Relations Institute.** *East African Med. J.* 1946, Dec., v. 23. No. 12, 361–84. [24 refs. & bibliography.]

DARLOW, H. M. **Freetown Memories.** *J. Roy. Nav. Med. Serv.* 1946, Oct., v. 32, No. 4, 263–9.

The author gives a "racy and breezy" description of his "enforced" sojourn in the immediate vicinity of Freetown in so far as the environment affected the health of the personnel of the naval base. It will be read with some pleasurable interest by any who know Freetown, but erroneous conclusions may be drawn by the reader unfamiliar with Sierra Leone. *R. Ford Tredre.*

BOOK REVIEW.

WORTHINGTON, E. B. **Middle East Science. A Survey of Subjects other than Agriculture. A Report to the Director General, Middle East Supply Centre, August, 1945.** pp. xiii+239, 16 pls. & 5 maps (2 folding). 1946. London: H.M. Stationery Office. [7*s.* 6*d.*]

The appointment of a Scientific Advisory Mission to the Middle East Supply Centre was made in 1943, the Centre itself being established by the British Government in 1941 and, in 1942, being joined by America, to ensure that the countries concerned were provided with "supplies which were essential for their livelihood in war-time." These countries consisted of an inner group comprising Egypt, the northern Sudan, Palestine, Transjordan, Lebanon, Syria, Iraq, and Cyprus, and an outer group comprising Persia, Saudi Arabia, Aden, Ethiopia, Eritrea, Somaliland, the southern Sudan, Cyrenaica, Tripolitania and Malta.

The members of the Mission were Dr. B. A. Keen, F.R.S., Dr. E. B. Worthington, Dr. H. B. Allen and Dr. N. C. Wright. Dr. Keen is Assistant Director of the Rothamsted Agricultural Experimental Station and has written a book, in the same series as the present, on *The Agricultural Development of the Middle East*; Dr. Worthington, author of the present volume on *Middle East Science*, is Director of the Freshwater Biological Association; Dr. Allen has written on *Rural Education and Welfare*, and Dr. Wright on *Animal Industry in the Middle East*. We are concerned here with the second of these. Many of the questions with which Dr. Worthington deals are of interest to countries outside the Middle East, since they treat of natural factors such as climate, soil and mineral resources, and with racial, cultural, religious, economic and social influences; hence the value of this record is not limited to the countries detailed.

The present report is arranged so as to treat of subjects rather than of the different countries and territories *seriatim*, and this is a wise measure. If each country were to be described separately with regard to each of the important questions, there could not fail to be much repetition and therefore loss of interest. By the arrangement adopted, the wide and important matters are discussed and illustrated by examples taken now from one, now from another, of the various countries. This may be a more difficult process of thought and writing, but it does tend to maintain interest. Those who have read and enjoyed Dr. Worthington's *Science in Africa* [this *Bulletin*, 1939, v. 36, 265] will expect a high standard in the present work and they will not be disappointed.

We will describe briefly the general plan of the work and then speak more specifically of the parts concerned with medical and hygienic problems, which will be of greater interest to readers of this *Bulletin*. The author starts with a

short chapter on *Basic Problems*, the stages of development, planning and political background, and passes on to *Surveys*, geodetic, topographic and cadastral, designed for determining property boundaries for purposes of land settlement and sequent registration and taxation. *Geology* and *Meteorology* come next, followed by the various sources of *Water Supply*, by rivers, underground water (wells and springs) and storage and domestic supplies for man and stock. *Plants and Animals*, and relations of research to economic ends, ecological surveys and conservation of wild life, and *Forestry* and its importance follow. Next, *Marine and Inland Fisheries*, the systems of the Nile, the Tigris and Euphrates, and the Rift Valley, their resources and stages of development, irrigation and food problems connected therewith. Three chapters, of which more will be said later, are concerned directly or indirectly with medical and public health problems, and preceding the final Review chapter is one on *Population* and *Social Studies*.

The scope of the work, it will be seen, is very wide, and the illustrations afforded by the different countries and adduced to force home points stressed have been carefully and aptly chosen.

Passing to a consideration of medical questions in rather more detail, the author has divided human diseases into those of environment, such as malaria, yellow fever, trypanosomiasis, leishmaniasis, sandfly fever, onchocerciasis and the like ; next, disease due to or associated with insanitary conditions or bad habits, such as schistosomiasis, ankylostomiasis, cestodiasis and other helminthic infestations, louse-borne disease, as typhus and relapsing fever, eye diseases, enteric fevers and dysentery. Tuberculosis, smallpox, leprosy and venereal diseases are also discussed, and the question of narcotics and the opportunities for research and investigation into branches of forensic medicine.

Malaria is largely responsible for retardation in the progress of education, agriculture and social welfare. *A. gambiae* is the most important vector in tropical Africa and in the southern part of the Middle East area including West Arabia ; *A. maculipennis* (especially *sacharovi*) in Mediterranean countries ; *A. superpictus* in the hills of Cyprus and the Levant ; *A. sergenti*, and *A. claviger*, which transmits infection in the urban districts of Palestine, owing to its habit of breeding in cisterns used for water-storage. Though agriculture at times results in diminution of malaria prevalence, it may, from irrigation, cause an increase. The date-growing country near the Shatt-el-Arab offers opportunities for a combined scheme for water control, agricultural improvement and suppression of malaria. Intermittent drying is mentioned, and the connexion between it and agricultural practice and malaria in rice-growing areas of Lower Egypt, where the vector is *A. pharoensis*, but though theoretically valuable it may not always be practical because water is not available at all times when it is required. The dangers of major engineering works, construction of dams and flooding of land, are not forgotten.

The outcome of immunity surveys in proving areas of existence of *yellow fever* is referred to, showing that the disease should be regarded as endemic throughout the Sudan south of about latitude 15°N., and that the disease has recently occurred as far east as the Ethiopian border and in the western plains of Eritrea bordering the Sudan. The dangers of the Red Sea ports becoming centres for distribution of the infection by shipping and dhow traffic in which mosquito control is, to say the least, difficult, are all stressed. Mention is made of the methods of control of *trypanosomiasis* in the southern Sudan. *Onchocerciasis* prevails in Ethiopia and the southern Sudan.

Urinary schistosomiasis is essentially a disease associated with irrigation lands and insanitary habits ; the rectal form is not yet common in some of the countries surveyed, but is said to be increasing. In Iraq, the former only occurs and then mainly in the marsh areas of the south, because the irrigation water is turbid

and rooted vegetation slight and snails few; the same may be said of the plains of Khuzistan in south-west Persia. *Hookworm* is rife in Egypt, as are other helminths, notably *tapeworms*. The fly problem is closely bound up with *eye diseases* and with *typhoid fever* and *dysentery*. All these medical conditions are touched upon, but the information is already known to readers of this *Bulletin*; the book is not intended for specialists in medical problems, but for the educated layman, and consequently details on these subjects are beyond the strict scope of the work.

Studies undertaken in different parts of the Middle East show that, speaking generally, the area is among the worst-nourished parts of the world; 70 per cent. or even more of the diet energy comes from cereals and roots. In irrigated areas there is malnutrition from imbalance of diet, while nomads and those with small reserves suffer from innutrition amounting at times to actual starvation after bad seasons. Common deficiency diseases are anaemia, rickets, pellagra, osteomalacia and eye affections.

As regards *Health Services*, more hospital beds are needed, the present ratio per population is very low. Most of the countries have one or more laboratories for public health services and for research. There are nine medical schools in existence, some with dental schools attached. Only Cyprus, Transjordan, Ethiopia and the former Italian colonies are without medical schools. Most of the men who qualify from these schools stay in the towns, so rural areas are poorly served. The training of subordinate grades, sanitary inspectors, midwives, dispensers, nurses and dressers, has come to the fore but recently. The question of training men and women for a grade in Government Service intermediate between the medical officer and the sanitary inspector or dispenser is mentioned. Training of midwives and nurses is an acute need and is hampered by racial or religious prejudice. Finally, the establishment of a regional branch of the International Health Office, controlled by a committee selected by all the countries concerned, would be of great help, especially if it were followed up by periodic conferences at which medical and health problems could be discussed. [This Office is now superseded by the United Nations Organisation.]

Above are some of the subjects debated and discussed in this book, and appended to the work is a fairly full list of references and, what is rare nowadays, a list of the principal persons who have assisted the author with information. Both the last furnish abundant evidence that much study and thought have gone to the writing of this book; references to books, articles, papers and pamphlets number 200 and the list of those consulted personally by the author comprises nearly 250. There are plates with interesting photographs well reproduced, and maps in the text illustrating rivers, irrigated lands and swamp areas, and two detailed coloured maps at the end of the work. The only inadequate and unsatisfactory part of the whole is the Index, which, to serve any useful purpose, should be full and detailed. This could easily be remedied in a future edition.

H. Harold Scott.

Printed under the authority of His Majesty's Stationery Office
by The South Essex Recorders, Ltd., Ilford.

(178) Wt. P11/325 6/47 S.E.R. Ltd. Gp. 432.

ALPHABETICAL LIST OF AUTHORS OR SOURCES.

Abbott, P. H., 506.
d'Andurain, C. W., 511.
Angel Torrico, M. R., 510 *bis*.
Ann. Trop. Med. & Parasit., 498 *bis*, 499 *bis*.

Bachi, R., 542.
Bacigalupo, J., Rey, M. & Toce, A., 529.
Bang, F. B., Hairston, N. G., Maier, J. & Trager, W., 503.
Bannerman, H. C., 547.
Bell, E. J., Bennett, B. L. & Whitman, L., 514.
Bénard, H., Rambert, P., Cajdos, A. & van den Broucke, 533.
Berke, Z., 512.
Berkowitz, A. P., 513.
Bhattacharji, L. M., Singh, J. & Sen Gupta, G. P., 546.
Blanc, F. & Siguier, F., 524.
Bloss, J. F. E., 527.
British Guiana, 504.
Brown, M. & Rennie, J. L., 497.
Byrne, E. A. J., 537.

Calero, C., 525.
Cantacuzène, A. & Lupasco, G., 529.
Catanei, A., 536.
Chesterman, C. C., 527.
Ciaravino, E. & Sofia, F., 495.
Codeleoncini, E., 512.
Corcoran, A. C. & Page, I. H., 539.

Darlow, H. M., 548.
David, W. A. L. & Bracey, P., 544.
van Dyke, H. B. & Gellhorn, A., 512.

Fairbairn, H. & Burtt, E., 506.
Fairley, N. H., 538.
Fedorov, V. G., 544.
Fenner, F., 514.
Findlay, G. M., 527.
——, Maegraith, B. G., Markson, J. L. & Holden, J. R., 501.
Floch, H., 486.
Fonseca, F., Cambournac, F. J. C., Pinto, F. M. R., Pereira, J. M. & Cunha, A., 487.
da Fonseca Santos, H. S., 506.

Gage, J. C. & Rose, F. L., 500.
Gelfand, M., 539.
Gevorkov, A. A., 486.
Giglioli, G., 504.
Ginés, A. R. & Poletti, J. G., 528.
Girard, G., 520.
Goldsmith, K., 502.
Grasset, E., 520.
Guyane Française, 486.

Hackett, C. J., 527 *bis*.
Haddow, A. J., Gillett, J. D. & Highton, R. B., 516.
Heilig, R., 512.
Henderson-Begg, A., 509.
Hernando Ordóñez, J., 532.
Hewer, T. F., 527.
Hoffman, W. H., 517.

d'Ignazio, C. & Codeleoncini, E., 526, 539.
Ivanova, L. V., 488.

Johnson, C. G., 545.
Johnstone, R. D. C., 530.
Jones, H. A., Incho, H. H. & Deonier, C. C., 504.

Katzeneilenbogen, I., 539.
Kessel, J. F. & Moore, F. J., with Kaplan, F. M. & Schireson, R., 524.
Kierland, R. R., 499.
King, W. V. & Hoogstraal, H., 543.

Knoll, E. W. & Howell, K. M., 524.
Koprowski, H. & Cox, H. R., 518.

Lange, H. F., 547.
Launoy, L. & Prieur, M., Mlle., 509.
Leech, R. B., 527.
Lewis, C. F. & Musselman, M. M., 531.
Lum, L. C., 500.

Macchiavello, A., 519.
Mackerras, I. M., 513.
Madden, A. H., Schroeder, H. O., Knipling, E. F. & Lindquist, A. W., 544.
Maegraith, B. G., *et al.*, 498 *bis*, 499 *bis*.
——, Tottey, M. M., Adams, A. R. D., Andrews, W. H. H. & King, J. D., 501.
Malone, R. H., 511.
Marikovski, P. I., 503.
de Meillon, B. & Golberg, L., 525.
Meleney, H. E., 492.
Mer, G., Birnbaum, D. & Aioub, A., 542.
Most, H., Kane, C. A., Lavietes, P. H., London, I. M., Schroeder, E. F. & Hayman, J. M., 496.
Mukhatcheva, O. N., 494.
Murgatroyd, F., 527.

Oliver-González, J., 529.

Payne, E. H., Balthazar, E. & Bezerra, D. A., 502.
——, —— & Fernandes, J. S., 502.
Petrjaev, E. D., 515.
Pinedo, C., Cánepa, C. H. & Fukelman, R., 532.
Pinilla B., C., 529.

Rail, G. A., 522.
Rice, R. I., Johnstone, H. F. & Kearns, C. W., 544.
Rigdon, R. H. & Varnadoe, N. B., 505.
Ross Institute of Tropical Hygiene, India Branch, 547.
Rotenburg, S. S., 515.

Sagher, F., 539.
Sanjuan Fuentes, J., 486.
Schwetz, J., 503.
Sergent, Et., 534, 535 *bis*.
Shamanna, D. & Hedge, K. V., 520.
Shortt, H. E., 511.
Shute, D., 521.
Silva, M. S., 538.
Simons, R. D. G. P., 535.
Smadel, J. E., Jackson, E. B., Bennett, B. L. & Rights, F. L., 513.
Smith, C. E., Beard, R. R., Rosenberger, H. G. & Whiting, E. G., 537.
Spies, T. D. & Stone, R. E., 533.
Stannus, H. S., 527.
Stubenbord, W. D., 528.
Sullivan, C. J. & Broun, G. O., 532.

Taliaferro, W. H., 493.
Tredre, R. F., 488.
Trupp, M., 495.

Ustinov, A. A., 490, 491.

Watson, J. M., 524.
Watts, J. C., 527.
Wenyon, C. M., 527.
Wharton, G. W., 545.
White, R. Senior & Rao, V. V., 491.
Wicht, J. F. & Rabkin, R., 514.
Williams, M. H. C., 526.
Worthington, E. B., 548.
Wylie, J. A. H., 526.

Young, M. D., Ellis, J. M. & Stubbs, T. H., 492.

Zuckerman, A., 504.

ISSUED UNDER *the* DIRECTION *of the* HONORARY MANAGING COMMITTEE *of the* BUREAU *of* HYGIENE *and* TROPICAL DISEASES.

BULLETIN OF HYGIENE

Containing abstracts of current medical literature on public health administration, social services, communicable diseases, sanitation, nutrition, industrial hygiene, bacteriology and immunity, and related subjects of public health interest.

ISSUED MONTHLY.

Subscription: 30*s.* a year, post free.

Orders and Subscriptions should be sent to—

THE BUREAU OF HYGIENE AND TROPICAL DISEASES,

Keppel Street, Gower Street, W.C.1.

HEALTH HORIZON

—a Magazine for Doctors and Laymen

Containing articles by well-known writers on Health and Social problems at home and abroad.

CURRENT ISSUE:

Does Athletics Injure Health?
Sir Adolphe Abrahams

The Locusts Are Coming:
Harley Williams

Quarterly: One and sixpence per copy
Five shillings per year

HEALTH HORIZON,
Tavistock House North,
Tavistock Square,
London, W.C.1.

Publications of the Bureau of Hygiene and Tropical Diseases.

TROPICAL DISEASES BULLETIN

containing classified summaries of current papers and reports from the medical and scientific publications of the world on diseases of the tropics and warm countries.

(ISSUED MONTHLY.)

Subscription rate (in advance): 30 shillings per annum, post free. The subscription runs from January to December. Single numbers 3s. 6d. each.

BULLETIN OF HYGIENE

containing abstracts of current medical literature on public health administration, social services, communicable diseases, sanitation, nutrition, industrial hygiene, bacteriology and immunity, and related subjects of public health interest.

(ISSUED MONTHLY.)

Subscription rate (in advance): 30 shillings per annum post free. The subscription runs from January to December. Single numbers 3s. 6d. each.

ORDERS and SUBSCRIPTIONS may be sent direct to the

BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street,
Gower Street,
London, W.C.1.

or through any bookseller.

Cheques and Postal Orders should be made payable to the "Bureau of Hygiene and Tropical Diseases," and crossed "Westminster Bank Ltd."